Vol. 30 No. 6 Abstr. 1340–1609 December, 1961

ABSTRACTS OF WORLD MEDICINE

A Monthly Critical Survey
of Periodicals in
Medicine and its Allied Sciences

LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION £4.4.0 U.S.A. AND CANADA $13.50 SINGLE NUMBER 8/6

ABSTRACTS OF WORLD MEDICINE

It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medic periodicals published in every part of the world, and in this way to enable him to keep in touch with new develop ments throughout the whole field of medicine and in each of its special branches, including those aspects of surger which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appe to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted i sufficient detail to indicate to the general reader the nature and value of that contribution and to enable th specialist to assess its importance in relation to his own work and to decide whether the original article should b read in full. The author's own summary or an editorial summary published with the original article may occasion ally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order t draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealin with medical and surgical aspects of the same problem appear together. The titles of papers written in language other than English are given both in translation and in the original form. The titles of journals are given in full an also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standard Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). Th transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: Inter national System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

ABSTRACTS OF WORLD MEDICINE

VOL. 30 NO. 6 DECEMBER, 1961

Pathology

1340. **Measurement of Urinary Protein**
B. LEWIS and P. RICHARDS. *Lancet* [*Lancet*] **1**, 1141–1143, May 27, 1961. 1 fig., 6 refs.

A comparison of the Esbach procedure for measuring urinary protein with a turbidometric method using the Medical Research Council grey-wedge photometer was made at St. George's Hospital, London. Samples for analysis were prepared by adding known weights of dried albumin in varying concentrations to normal urine. It was found that the turbidometric method gave much more accurate and reproducible results; the procedure is rapid, simple, and suitable for use in the ward.

H. Harris

1341. **Gastrointestinal Lesions in Starvation Induced by Drugs or Simple Food Reduction**
J. A. NISSIM. *Lancet* [*Lancet*] **2**, 132–135, July 15, 1961. 6 figs., 12 refs.

The author had previously observed that large doses of trimethylhexadecylammonium stearate and related compounds given to experimental animals in large doses produced ulceration and haemorrhages in the gastro-intestinal tract and that long-term administration of smaller doses produced similar gastro-intestinal lesions and led to gross inanition. In this paper from Guy's Hospital Medical School, London, he describes experiments designed to ascertain whether the lesions in the latter type of experiment were due to a direct toxic effect of the drug or a manifestation of the associated inanition.

Lesions produced in 38 drug-treated mice (12 received 0·4% trimethylhexadecylammonium stearate, 14 0·5% trimethylhexadecylammonium stearate, 6 0·2% cetrimide, and 6 0·4% cetrimide incorporated in a standard diet, of which each mouse received 5 g. daily until death) were compared with those obtained in 32 mice given from 1 to 3·5 g. daily of the diet alone until they died. Similar dietary restriction experiments were undertaken on 4 rats, 4 guinea-pigs, and 4 rabbits.

The mice in each group showed no significant difference in the degree of loss of weight; the frequency of gastro-intestinal haemorrhages was also similar, occurring in 25 of 32 (78·1%) and 30 of 38 (78·9%) of the starved and drug-treated animals respectively. The distribution of the lesions, starting in the stomach and involving the duodenum, jejunum, and often the whole of the ileum, was similar in the two groups. Microscopically, there were multiple areas of mucosal ulceration in the stomach and the tips of the small intestinal villi were abnormal in association with the haemorrhages. Lesions were slight in the guinea-pigs; they occurred in the stomach and the whole of the small intestine in the rats, and in the rabbits were confined to the stomach.

It is considered that the differences in the distribution and severity of the lesions in the different species are more likely to be related to the generation time of the mucosal cells rather than to any associated vitamin deficiency and that the lesions occurring with the administration of the drug are explicable by the inanition which it produces and are not due to a direct toxic effect of the drug.

Hewett A. Ellis

1342. **A Capillary Test for "L.E." Cells**
P. MUDRIK, C. L. LEE, and I. DAVIDSOHN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **35**, 516–519, June, 1961. 2 figs., 5 refs.

A micromethod of detecting lupus erythematosus (L.E.) cells is described. Heparinized capillary tubes (1·5 by 75 mm.) are filled to three-quarters of their capacity with blood from the finger or ear, sealed with modelling clay, and centrifuged in a haematocrit centrifuge. The plasma and buffy coat are mixed thoroughly with a fine wire and the tubes incubated for 2 hours at room temperature or 30 minutes at 37° C. The tubes are centrifuged again and then broken about 2 mm. below the buffy coat layer, which is expressed on to a slide, care being taken to avoid transferring excess plasma with it. Smears are obtained by gently placing a second slide on top of the first and separating them while keeping the two slides parallel, the smears being then stained with Wright's or Giemsa's stain.

At Mount Sinai Hospital, Chicago, the results obtained with the capillary technique were compared with those of the clot method of Zimmer and Hargreaves (*Proc. Mayo Clin.*, 1952, **27**, 424). Tests on 24 patients in whom systemic L.E. had been clinically diagnosed showed the presence of L.E. cells by the capillary method in 20 and by the clot method in 17. L.E. cells were found in 7 out of 18 patients with rheumatoid arthritis by the capillary method compared with 5 by the clot method. No L.E. cells were found by the capillary method in blood from 300 patients with other diseases.

The main advantages claimed for the technique are that only a small amount of blood is used and no special equipment is needed. The incubation is performed in a minimum of space, which should help phagocytosis, and in making the smears practically all the L.E. cells are concentrated in a small area, thus facilitating microscopical examination.

A. E. Wilkinson

1343. **Fluorescent Antibody Procedure for Lupus Erythematosus: Comparative Use of Nucleated Erythrocytes and Calf Thymus Cells**
D. WIDELOCK, G. GILBERT, M. SIEGEL, and S. LEE. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **51**, 829–835, June, 1961. 4 figs., 9 refs.

Working at the laboratories of the City Department of Health, New York, the authors have compared the results of three diagnostic tests for systemic lupus erythematosus (S.L.E.) on a large number of sera from 63 patients with S.L.E., 48 with rheumatic diseases, 471 with arthritis, 46 with other diseases, and 1,400 with syphilis. The tests used were the L.E. cell test and two fluorescein antibody techniques using as nuclear material fresh calf thymus nuclei and chicken erythrocytes respectively.

Of the 63 cases of S.L.E., 84% gave a positive reaction in the calf thymus test compared with 74% in the L.E. cell test and 37% in the chicken cell test. Among the 48 patients with rheumatic diseases the incidence of positive results was 33·3% in the calf thymus test, 10·4% in the L.E. cell test, and 4·1% in the chicken cell test, these false positive results occurring mainly in patients with rheumatoid arthritis. Tests on 237 relatives of the patients with S.L.E. were positive in 3·3% with the calf thymus test and in 0·8% with the L.E. cell test, but were invariably negative with the chicken cell test. All tests on relatives of patients with other diseases gave negative results.

Because of the higher incidence of positive results and the lesser degree of specificity the authors recommend the calf thymus test as a screening test for systemic lupus erythematosus and reserve the more specific chicken erythrocyte test for confirmation in doubtful cases.

M. Wilkinson

HAEMATOLOGY

1344. **Electron Microscopic Study of Leukocytes in Infectious Mononucleosis**
R. D. PAEGLE. *Blood* [*Blood*] **17**, 687–700, June, 1961. 20 figs., 24 refs.

From Yale University School of Medicine, New Haven, Connecticut, is reported a study by both light and electron microscopy of the leucocytes from 8 patients with infectious mononucleosis, one with chronic lymphocytic leukaemia, and 3 healthy individuals. The majority of the mononuclear cells in the cases of infectious mononucleosis belonged to the lymphocytic series, but a small number of the cells when examined by the electron microscope showed more endoplasmic reticulum and smaller mitochondria than the average lymphocyte, suggesting that they were monocytes. Comparison of the electron-microscopic appearances of the abnormal lymphocytes with the appearances seen in Wright-stained smears demonstrated that it was not possible to classify the lymphocytes with the electron microscope as is possible with the light microscope. Only one cell which appeared to correlate with a Downey type was seen; this was similar to Downey Type 11—that is, the large cell with abundant pale cytoplasm. The mitochondria in the lymphocytes from patients with infectious mononucleosis were generally larger and more varied in shape than those from healthy subjects. There was considerable variation in the density of the cytoplasm in the abnormal cells, presumably due to the presence of PNA granules (granules of Palade). But the fact that the appearances varied so much from cell to cell, together with the occasional appearance of abnormal features in normal cells, made it unjustifiable to attempt a classification of lymphocytes as atypical or typical on the basis of electron-microscopic examination. One of the objects of the investigation was to look for possible inclusion bodies suggesting a viral agent as the cause of infectious mononucleosis, but no bodies suggestive of virus inclusions were observed. Lymphocytes similar to those seen in infectious mononucleosis also occur in other diseases of definitely viral aetiology, but the presence of these abnormal cells may mean a reaction to a variety of stresses rather than a specific reaction to a virus.

R. F. Jennison

1345. **Platelets in the Thromboplastin Generation Test: Electron Microscopic Studies**
G. B. HAYDON and D. L. COREY. *Archives of Pathology* [*Arch. Path.*] **71**, 615–620, June, 1961. 2 figs., 10 refs.

This paper from Stanford University, California, describes electron-microscopic studies of platelet morphology during the course of incubation of the reconstituted substrate of the thromboplastin generation test, while stored in a stable saline suspension, and in clotting fresh whole blood. The authors find that platelets in a stable preparation show little morphological change during a week of storage at 4° C. The progressive changes in platelet form, known as viscous metamorphosis, which occur in the reconstituted substrate of the thromboplastin generation test resemble those occurring in fresh blood. It is concluded that platelets are playing the same role in both processes. The paper provides support for the usefulness of the thromboplastin generation test as a model clotting system in the study of coagulation disorders.

A. Brown

1346. **Rapid Selection of Group A Recipients among Mass Casualties**
P. D. STEWART. *British Medical Journal* [*Brit. med. J.*] **2**, 93–94, July 8, 1961. 6 refs.

In the introduction to this paper from the Vale of Leven Hospital, Alexandria, Dunbartonshire, it is argued that rapid recognition of Group-A recipients among mass casualties would allow available Group-O blood to cover almost twice as many cases as at present. The author has carried out three trials to test the feasibility of rapid selection of such recipients under field conditions by means of Zeitlin's test, in which a drop of tap-water and a drop of the recipient's blood are mixed on a slide coated with potent anti-A serum. Trials 1 and 2 were carried out under black-out conditions in a reception tent with poor illumination and a casualty admission rate of approximately one a minute. The observers, who were experienced laboratory technicians, often had considerable difficulty in deciding whether agglutination was

present or not in Trial 1; in Trial 2, however, electric head lamps were used and this made agglutination, when present, obvious. In Trial 3 liquid anti-A serum was used and the tests were read by unskilled personnel, using head-lamps when working after dark. In addition, in all three tests blood samples were taken into glucose-citrate and tested under laboratory conditions.

In Trial 1 there were 10 major errors, a Group-O or -B recipient being classified as Group A, in 84 tests. In Trial 2 there was one major error in 100 tests and in Trial 3 (178 tests) there were none. Minor errors, agglutination being missed when present, occurred twice in Test 1 and 3 times in Test 2. Most of the major errors in Test 1 were considered to be due to poor illumination and "faulty planning and recording of results". If this test is excluded the incidence of serious error in 278 tests was 0·3%. The method is therefore not free from risk, but in certain circumstances such a risk might be justifiable. It is emphasized that this is an emergency procedure designed to conserve blood supplies and one to be used only in circumstances in which full blood grouping and cross-matching are impracticable.

F. Hillman

MORBID ANATOMY AND CYTOLOGY

1347. **Viral Hepatitis under the Electron Microscope**
B. GUEFT. *Archives of Pathology* [*Arch. Path.*] **72**, 61–69, July, 1961. 11 figs., 9 refs.

An unselected group of needle biopsy specimens of the liver obtained from 48 patients at the Veterans Administration Hospital, Cincinnati, were examined by electron microscopy. Of 19 specimens from patients with virus hepatitis, 5 showed cytoplasmic particles. Small particles, about 400 × 600 Å in size, were observed in specimens from 3 patients with serum hepatitis, whereas large particles, 2,000 Å in diameter, were found in a further 2 patients. One of the last 2 patients was believed to have epidemic hepatitis, but was receiving isoniazid and streptomycin for tuberculosis, while the other had recurrent hepatitis of 2 years' duration. It is suggested that the particles represent the virus agents of hepatitis.

[It is of interest that particles were found only in severe hepatitis and that they could not be seen in liver biopsy specimens from 14 patients with a milder form of the disease.]

D. Geraint James

1348. **An Exfoliative Cytologic Study of Intracranial Fluids**
B. NAYLOR. *Neurology* [*Neurology* (*Minneap.*)] **11**, 560–570, July, 1961. 10 figs., 17 refs.

Experience of exfoliative cytology in the study of intracranial fluid is described in this paper from the University of Michigan Medical Center, Ann Arbor. A total of 68 specimens of cerebrospinal fluid (C.S.F.) (66 from the lateral ventricle and 2 from the cisterna magna) and 10 specimens of cyst fluid were examined by two techniques—the serum-toluidine blue wet film of McCormack *et al.* (*Cancer*, 1957, **10**, 1293) and the wet-fixed smear stained by Papanicolaou's method.

Tumour cells were detected in C.S.F. from 5 out of 31 patients with malignant intracranial neoplasms, in cyst fluids from 2 patients with malignant tumours, and in pituitary cyst fluid from one patient. Of 8 specimens of C.S.F. from cases of metastatic intracranial neoplasm, tumour cells were recovered from 3. A porencephalic cyst aspirate was found to contain ciliated columnar cells.

In the author's experience there has been no difficulty in differentiating between cells of epithelial and those of gliomatous origin.

H. S. Schutta

1349. **The Problem of Malignancy in Ependymomata.** (К вопросу о злокачественности эпендимом)
T. P. VERHOGLJADOVA. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **61**, 504–508, No. 4, 1961. 3 figs., 17 refs.

There is much divergence of opinion as to the malignancy of ependymomata, some authors denying it and others regarding all such tumours as malignant and infiltrative. On the basis of her study of 80 cases of cranial and spinal ependymoma the present author takes a middle course. Over half (48) of these tumours arose in the 4th ventricle, 4 in the 3rd ventricle, 7 in the lateral ventricles, 5 (intramedullary) in the spinal cord, and 16 (extramedullary) in the cauda equina. She classifies them as typical (53 cases), atypical (24), and malignant (3).

In the typical type of tumour the cells are monomorphic, the nuclei moderately full of chromatin, and mitosis is absent. The cells are usually arranged in perivascular "pseudo-rosettes", or more rarely in true rosettes, there is a moderate number of blood vessels of adult type, and no necrotic areas are present. In the atypical type, rosettes are rare, the cells being irregularly scattered, there is polymorphism, and giant cells with hyperchromic deformed nuclei are present in small numbers, while in the blood vessels there is active hyperplasia of endothelium. In the small malignant group the above abnormalities are more pronounced, vacuolization and degeneration of the nuclei and mitosis are present, and wide areas of necrosis are found. In these malignant tumours the spread of growth is infiltrative, whereas that of the typical group is described as "expansive-infiltrative", that is, there is a sharp line of demarcation, but microscopically tumour cells can be seen extending into the surrounding nerve tissue.

Bailey and Cushing at first distinguished ependymomata from ependymoblastomata, but later rejected the latter term. The present author agrees that this term is not justified in practice, since there is no sharp distinction between the apparently innocent tumour and the obviously malignant type. The degree of cataplasia is reflected in the rate of growth of the tumour, and the atypical form is met with more often in younger patients (under 20 years). Furthermore, the tumour does not remain constant and has been observed to increase suddenly, with the development of metastases from a tumour previously considered to be benign. These tumours should therefore all be regarded as potentially malignant.

L. Firman-Edwards

Microbiology and Parasitology

1350. **Inoculation of Human Volunteers with a Strain of Virus Isolated from a Common Cold**
M. L. Bynoe, D. Hobson, J. Horner, A. Kipps, G. C. Schild, and D. A. J. Tyrrell. *Lancet* [*Lancet*] **1**, 1194–1196, June 3, 1961. 1 fig., 14 refs.

In an investigation at the Medical Research Council's Common Cold Research Unit, Salisbury, and the Virus Research Laboratory of the University of Sheffield 54 volunteers were inoculated by nasal drops or by nasal, conjunctival, or throat swabs with nasal washings obtained from volunteers with experimentally produced colds. Evidence of human transmission was sought by clinical observation and virus isolation and from serological antibody responses. Virus isolation from throat or nose swabs was attempted by inoculation of monkey kidney cell tissue culture. The neutralizing capacity of serum was estimated by measuring the reduction of the ability of a virus to produce microplaques after incubation with various dilutions of inactivated serum.

Colds were induced in 16 volunteers, mainly those inoculated by nasal washings, but also in 2 of 7 inoculated by nasal swabs and in 2 of 7 inoculated by conjunctival swabs. No colds were induced when the inoculum was applied to the throat. Virus was isolated from 13 of the 16 volunteers developing colds and from 12 of 14 showing rises in antibody titre. Volunteers who developed colds had low serum antibody levels before inoculation and usually developed high levels afterwards. Those who did not develop colds had higher pre-inoculation serum antibody levels, suggesting that circulating antibody provided resistance to a superficial mucous membrane infection. Accordingly it is suggested that vaccination might prove an effective prophylactic measure.

D. Geraint James

1351. **The Role of a Filterable Virus in the Aetiology of Rheumatic Fever.** (О роли фильтрующегося вируса в этиолопии ревматизма)
N. N. Vorob'eva and G. D. Zalesskij. *Вопросы Вирусологии* [*Vop. Virusol.*] **7**, 268–273, May–June, 1961. 6 figs.

In 1958 the authors first reported the isolation of a cytopathogenic virus from the blood, throat gargle fluid, and vegetations on the heart valves in cases of rheumatic fever. In these earlier studies, which are here briefly recapitulated, the successful cultures had been carried out with trypsinized human embryo fibroblasts. In the present study the answers to two questions were sought: (1) could the virus isolated from patients with rheumatic fever be the causative agent of a different infectious disease?; and (2) does it belong to some known group of viruses, such as the adeno- or enteroviruses, which happened to be present but latent in the patients?

During 1959, of 16 fresh strains of the virus isolated from patients with active rheumatic fever, 9 were recovered from the blood, 3 from the throat, one from the faeces, 2 post mortem from the kidneys and spleen respectively, and one from the left auricle during valvotomy. In 2 of these cases the virus was isolated at the beginning and again at the end of an acute phase of the disease lasting 9 and 7 months respectively. The cytopathogenic effect of each of the 16 strains on human embryo fibroblasts was not neutralized by antisera against Coxsackie virus A9, E.C.H.O. virus Types 1, 2, 3, 6, 8, 11, and 19, or poliomyelitis virus Types 1, 2, and 3. The authors' new virus thus does not appear to belong to any of the known enteric viruses. [An answer to the question regarding adenoviruses does not appear to have been sought.]

Further, during 1959 paired sera were taken from 26 patients with rheumatic fever and used in neutralization experiments on human fibroblast tissue cultures infected with virus Strain 311, which had an infectious titre of $1:10^6$. These tests showed that antibodies were present in 21 sera, the other 5 showing no protective antibody in either the first or the second serum sample. Neutralizing titres varied from 1:10 to 1:80; rising titres were observed in 5 out of 9 fresh cases, the increase being 2-fold in 2 cases, 4-fold in 2, and 8-fold in one. Of 8 relapsed cases, a 2-fold increase was obtained in 3 and a 4-fold increase in 2.

K. Zinnemann

1352. **Use of the Tissue Culture Method in the Study of Rheumatic Fever.** (Применение метода тканевых культур в изучении ревматизма)
T. A. Rubina. *Вопросы Вирусологии* [*Vop. Virusol.*] **7**, 284–285, May–June, 1961.

The author reports that all attempts to repeat the findings of Zalesskij and Vorob'eva, who claimed [see Abstract 1351] to have isolated a cytopathogenic virus from patients with rheumatic fever, have failed in his hands. Negative results were obtained both with fibroblast cultures in plasma and with trypsinized human embryo fibroblast cultures inoculated with serum or blood from 27 acute cases of rheumatic fever.

K. Zinnemann

1353. **Detection of a Virus Isolated from Patients with Rheumatic Fever by Means of the Fluorescent Antibody Method in Tissue Cultures of Fibroblasts.** (Выявление вируса, выделенного от больных ревматизмом, в культуре фибробластов при помощи меченой флуоресцирующей сыворотки)
S. P. Šurin, V. E. Javorovskaja, and V. P. Lozovoj. *Вопросы Вирусологии* [*Vop. Virusol.*] **7**, 273–276, May–June, 1961. 4 figs., 10 refs.

The method described by Coons *et al.* of labelling with fluorescein *iso*cyanate antisera with a high neutralizing titre against the virus isolated from patients with rheumatic fever was used in this study to localize the

infective agent within individual cells in infected tissue cultures of fibroblasts. Fluorescent granules were found within the nucleus in the early stages. Later, similar granules were seen in the cytoplasm until practically the whole of the cytoplasmic space was filled with fluorescent material; at this stage the nucleus was fluorescing less or not at all. Three virus strains, namely, Nos. 401, 403, and 311 behaved in a similar way antigenically when tested by Coons's method.

K. Zinnemann

1354. **Pathology of Cells Infected with Virus Isolated from Patients with Rheumatic Fever.** (К патогенезу поражения клетки вирусом, выделенным от больных ревматизмом)

S. P. Šurin. *Вопросы Вирусологии* [*Vop. Virusol.*] 7, 277–280, May–June, 1961. 5 figs., 10 refs.

In this study commonly used histochemical methods were employed in the examination of tissue cultures of human fibroblasts infected with virus from patients with rheumatic fever. In the early stages of infection the cell content of ribonucleic acid (RNA) was found to be greatly increased, but later it decreased and finally was present only in the vicinity of the nucleus. There then appeared in the cytoplasm eosinophilic granules which were susceptible to the action of deoxyribonuclease (DNA) and ribonuclease; at the same time the nucleus showed a loss of DNA. As the virus continued to multiply in the cytoplasm Hodgkiss–McManus-positive granules were seen, indicating anaerobic glycolysis, effected presumably by the virus, as a result of which probably hyaluronic acid and other mucopolysaccharides of a toxic nature were produced.

Degenerative changes in similar tissue cultures induced by starvation or bacterial infection were of an entirely different nature, and these will be reported elsewhere.

K. Zinnemann

1355. **Distribution of the Virus Isolated from Patients with Rheumatic Fever in the Body of Experimentally Infected Animals.** (Распространение вируса, выделенного от больных ревматизмом, в организме экспериментально зараженных животных)

O. I. Pirogova. *Вопросы Вирусологии* [*Vop. Virusol.*] 7, 280–283, May–June, 1961. 3 figs., 6 refs.

The author describes an investigation in which 8 virus strains isolated from the blood, nasopharynx, heart muscle, and tonsils after tonsillectomy of patients with rheumatic fever were used for inoculating young rabbits by injection intravenously, intra-arterially, and into the paratracheal tissue. Two weeks later the rabbits were killed and suspensions of heart muscle, liver, spleen, brain, and blood were inoculated into tissue cultures of human embryo fibroblasts. In all, 15 strains were recovered after 5 to 7 passages through tissue cultures. These strains produced a cytopathogenic effect within 3 to 5 days and this effect could be neutralized by homologous antisera [apparently cross-neutralization was not tried].

Isolations from rabbit heart muscle were most frequent (7 out of 10 cases), from spleen and liver in 4 out of 8, from brain in 3 out of 6, and from blood in one out of 3 animals. The least number of isolations was obtained from rabbits inoculated intravenously. No virus strains could be isolated from 14 normal rabbits, of which 4 had been injected with uninoculated tissue culture medium.

K. Zinnemann

1356. **Isolation of Viruses from Children with Infectious Hepatitis**

E. V. Davis. *Science* [*Science*] 133, 2059–2061, June 30, 1961. 1 fig., 2 refs.

Cytopathologic agents were isolated from 14 of 22 Indian children involved in an outbreak of infectious hepatitis in Arizona. Isolation was made in a serially transplantable cell line originating from human embryonic lung. Efforts to identify these agents as known viruses, by utilizing standard techniques, have been unsuccessful.—[Author's summary.]

BACTERIA

1357. **Identification of Enteropathogenic *Escherichia coli* O111:B4 by Means of Fluorescent Antibodies.** [In English]

D. Danielsson and G. Laurell. *Acta paediatrica* [*Acta paediat. (Uppsala)*] 50, 339–345, July, 1961. 2 figs., 14 refs.

In a study reported from the University of Uppsala the γ-globulin fraction of rabbit antiserum against *Escherichia coli* O111:B4 was conjugated with lissamine rhodamine B 200 and used for the specific detection of this organism in faeces, conventional cultural methods being used on the same specimens. Faeces were collected during an epidemic of infantile diarrhoea due to this strain of *E. coli*; conventional cultures were positive with specimens from 9 infants on 15 occasions, while the fluorescent antibody technique, after culture of the faeces in broth for 6 to 8 hours, gave positive results with specimens from 15 infants and 1 nurse on 35 occasions.

With saline suspensions the fluorescent antibody technique gave positive results as often as faecal culture and took one hour compared with 48 hours for culture. Cultures of this strain of *E. coli* were still positive by the fluorescent antibody technique after several months' storage at −15° C. *E. coli* could still be detected by this technique when positive faeces were diluted 1:128 with negative faeces, whereas cultural methods failed with dilutions greater than 1:2. The authors conclude that in experienced hands the method is useful for rapid diagnosis during epidemics.

M. Lubran

1358. **Classification and Taxonomy of Dysentery Bacilli.** (О классификации таксономии дизентерийных бактерий)

E. D. Ravič-Birger, B. L. Troickij, and V. D. Gekker. *Журнал Микробиологии Эпидемиологии и Иммунобиологии* [*Ž. Mikrobiol. (Mosk.)*] 32, 25–27, June, 1961. 5 refs.

Ewing *et al.* have stated (*Int. Bull. bact. Nomencl.*, 1959, 9, 177) that differences in nomenclature make the investigations of Soviet authors in the field of micro-

biology of dysentery difficult to understand. This paper is intended to overcome some of these difficulties.

According to the Soviet classification the bacilli causing dysentery are divided into 4 species: *Shigella grigorievshigae*, *Sh. stutzeri-schmitzi*, *Sh. flexneri*, and *Sh. sonnei*, all with biochemical, fermentative, and serological differences. Some of these species possess variants which are classified as subspecies and types—thus Novgorodskaya and Semyonova discovered a subgroup of *Sh. grigorievshigae*, but at the time of their first publication had not been able to compare their strains with those from abroad. It is now known that the strains of Novgorodskaya and Semyonova are identical with those of Large and Sachs. The first and second species of the Soviet classification mentioned above correspond to Subgroup A of the classification of the International Shigella Centre. The numbering from 1 to 10 used in the latter classification includes in the same order genuine species such as *Sh. grigorievshigae* and *Sh. stutzeri-schmitzi* together with such variants as the bacilli of Large and Sachs (Novgorodskaya-Semyonova) which in the Soviet view are not constant.

In the Soviet classification the species *Sh. flexneri* has 3 subspecies, namely, *flexneri*, *newcastle*, and *boydii-novgorodskaya*. These correspond to the international Subgroups B and C, and are all variants of shigellae with common general biological characteristics, as acknowledged by Ewing in 1949 (*J. Bact.*, **57**, 33). However, their antigenic heterogenicity permits the separation of these subspecies; for example, *Sh. flexneri* and *Sh. boydii novgorodskaya* can be split into types which give cross-agglutinations within the subspecies, but possess well marked type-specific antigens. In the authors' view it would be inconvenient to increase the number of these type strains indefinitely by including variants which can either lose or regain one or the other antigen; in their opinion it would be better to have reference strains classified according to their type-specific antigens. Thus Strains 3B, 4B, and 1a could serve as valid reference strains and in this way strains named according to the Soviet nomenclature could be compared with those designated by the International Shigella Centre. As the results of Novgorodskaya and of Ewing *et al.* show, not all the types described by these authors agree with each other—notably in regard to the subspecies *Sh. boydii-novgorodskaya*—and this is a further argument in favour of the adoption of type-specific antigens as the basis for classification.

There is no disagreement regarding the international Subgroups B (*Sh. flexneri*) and C (*Sh. boydii*). However, the subgroup labelled under the international classification as Type 6 (*Sh. newcastle*) includes a number of types which are biochemically not uniform and have not been adequately investigated antigenically. This is dealt with in the Soviet classification by designating each subgroup as a subspecies. Subgroup D of the international classification corresponds to the species *Sh. sonnei* in the Soviet classification. So far as the latter is concerned it is suggested that types within the subspecies *Sh. flexneri* and *Sh. boydii* should in future be labelled with arabic numerals in order to facilitate easier comparison in further studies. *K. Zinnemann*

1359. **Rapid Isolation of Salmonellae from Faeces**
J. M. S. Dixon. *Journal of Clinical Pathology* [*J. clin. Path.*] **14**, 397–399, July, 1961. 19 refs.

The author of this paper from the Public Health Laboratory, Ipswich, describes attempts to isolate salmonellae from faeces within 24 hours, using solid media, replica plating, and fluid media incubated for different times and at different temperatures.

MacConkey's agar with 1:25,000 brilliant green, desoxycholate citrate agar, and the bismuth sulphite agar of Wilson and Blair were inoculated with faeces and incubated at 37° C. for 24 hours. Of 279 positive specimens, 189 were positive with MacConkey's agar, 146 with desoxycholate agar, and 94 with the bismuth sulphite agar. Dilution of the faeces before inoculation gave results in the same order but the number of isolations was appreciably reduced. Replica plating on a variety of selective media from a direct plate incubated for 6 hours did not enhance the isolation rate. When selenite F medium was inoculated with faeces and subcultured after 24 hours at 37° C. 68 out of 76 specimens were positive. Subculturing after only 6 hours at this temperature yielded 21 (27·6%) positive results, but subculturing after 6 hours at 43° C. increased the yield to 24 (31·6%).

The best results at 24 hours were obtained by a combination of direct plating on MacConkey's agar supplemented by selenite F subcultured to solid media after 6 hours at 43° C.; the number of isolations rose from 189 to 223, a significant increase. *A. E. Wright*

SEROLOGY AND IMMUNOLOGY

1360. **A Phase Contrast Microprecipitin Test with Poliovirus Antigens. I. Properties of the Antigens and Antibodies and Optimum Conditions for Reaction.** [In English]
H. J. Eggers and A. B. Sabin. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **11**, 120–151, 1961. 6 figs., 24 refs.

The authors, writing from the University of Cincinnati College of Medicine, describe experiments with a microprecipitin test with poliovirus antigens and antibodies in which the results were read by phase contrast microscopy. Rabbit immune heated sera were used as reference sera. The antigens usually consisted of infectious fluids from monkey kidney cultures infected with poliovirus Types 1, 2, and 3; for some tests, however, the antigens were prepared from a cell line of embryo rabbit kidney. The unconcentrated fluids were found to be relatively inactive and they were therefore concentrated 50 times by high-speed centrifugation. "Box titrations", requiring only 0·01 ml. of each reagent at each point, were performed on glass slides and were read by phase contrast microscopy after 4 hours' incubation at 36° C. In positive reactions there developed a characteristic precipitate, of which photomicrographs are presented. Details of the laboratory procedures are given.

Type-specific reactions in high titre were exhibited with rabbit immune sera. Heterotypic cross-reactions, when

they occurred, were at low serum dilutions only. Investigations were conducted to determine the optimum conditions for the microprecipitin reaction, and the results suggested that an extension of the period of incubation plus the use of unheated sera might be the procedure of choice for obtaining maximum titres. In experiments designed to obviate the handling of virulent live virus it was found that attenuated poliovirus strains provided satisfactory antigens of only slightly less potency than that of the virulent virus antigens; on the other hand heating the antigens to destroy infectivity rendered them non-reactive. Highly purified Type-1 poliovirus (Fraction D) reacted with rabbit immune serum in a manner similar to that of the concentrated virus antigen. Monkey immune sera known to contain neutralizing and complement-fixing antibodies and to give a positive precipitin reaction by the agar diffusion technique were examined by the microprecipitin test. Unexpectedly, the results were negative, except that some limited reactions occurred with Type-2 and Type-3 sera when these were used unheated. A preliminary investigation of specimens of sera from patients with poliomyelitis demonstrated the presence of microprecipitin antibody in such sera.

The authors present an informative survey of differences and similarities between their own findings and those of other workers and discuss problems regarding specific and possible non-specific factors involved in the reaction, inhibition zones, and the role of infective and non-infective virus. *Joyce Wright*

1361. **A Phase Contrast Microprecipitin Test with Poliovirus Antigens. II. Occurrence and Development of Microprecipitin Antibody after Natural Inapparent Infections, after Inoculation of Salk Vaccine, after Feeding of Attenuated Live Poliovirus Vaccine, and in Disease Caused by Polioviruses and Other Enteroviruses.** [In English]

H. J. EGGERS and A. B. SABIN. *Archiv für die gesamte Virusforschung* [*Arch. ges. Virusforsch.*] **11**, 152–175, 1961. 19 refs.

The authors employed the phase contrast microprecipitin test described in the first part of this paper [see Abstract 1360] in a study of the occurrence and development of poliovirus precipitin antibodies in the serum in man.

The reaction was negative in 11 healthy children and adults without neutralizing antibodies in their serum; it was positive in 7 (16%) of 44 naturally immune healthy persons, the reactions occurring only with sera containing neutralizing antibody of the corresponding poliovirus type. The microprecipitin reaction was positive in 32 (90%) of 36 patients with clinical poliomyelitis and poliovirus in their stools (Type 1 in 23 cases, Type 2 in 2, and Type 3 in 11). The reaction usually reached maximum titre within the first week after onset and began to decline a few weeks thereafter. The microprecipitin reactions were type-specific in those patients infected with poliovirus apparently for the first time; heterotypic reactions occurred frequently in patients with pre-existing heterotypic neutralizing antibodies, but the homotypic microprecipitin titres were usually higher than the heterotypic. The neutralizing antibodies generally appeared earlier than the microprecipitin antibodies and there was no correlation between their respective levels. These and other data suggest that the microprecipitin antibody is different from the neutralizing and complement-fixing antibodies.

Attenuated live poliovirus vaccine was given orally to 5 adults and to 5 children without pre-existing antibodies to the poliovirus type or types administered. The adults ingested Type-1 virus only and all of them developed Type-1 microprecipitin antibody, which was found to appear later than the Type-1 neutralizing antibody. The children ingested virus of Types 1, 2, and 3; against Types 1 and 2 they developed microprecipitin antibodies comparable in titre to those found in clinical poliomyelitis, but against Type 3 the titres in some cases were low. Microprecipitin response to Salk vaccine in children was less frequent and less marked, and it occurred most often in those with pre-existing neutralizing antibodies of the corresponding type. Investigation of patients with poliomyelitis and of patients infected with enteroviruses other than polioviruses indicated that Coxsackie A 9 and polioviruses may possess a minor microprecipitin antigen in common.

The authors examine the present position regarding the possible usefulness of the microprecipitin test and recommend that experience of its diagnostic significance should be enlarged. Discussing the criteria required in its interpretation, they conclude that " in a person, who was not vaccinated against poliomyelitis in recent months with either live or killed poliovirus vaccine and presents clinical manifestations compatible with poliomyelitis, a high titer (16 or over) of precipitin antibody at 7 to 14 days after onset would carry with it a high probability of current infection with poliovirus ". *Joyce Wright*

1362. **The Complement Fixation Reaction for the Early Diagnosis of Poliomyelitis.** (La réaction de fixation du complément pour un diagnostic précoce de la poliomyélite)

J. VIRAT. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **101**, 125–132, July, 1961. 5 refs.

At the Institut Pasteur, Paris, the value of the complement fixation test for the early diagnosis of poliomyelitis was investigated in 284 patients, from whom specimens of faeces were also examined for presence of the virus. The antigens for the test were prepared from the strains of virus cultured in KB cells and were used both heated and unheated.

Virus was isolated in 132 cases and a positive complement fixation reaction was obtained in 84% of these. Sera from 20 cases of respiratory disease gave negative results, as did also 3 sera from patients from whom another type of enterovirus was isolated. It is concluded that a single specimen of serum collected within 15 days of onset of symptoms and yielding a positive complement fixation reaction is considered sufficient grounds for suspecting poliomyelitic infection. *J. E. M. Whitehead*

Pharmacology and Therapeutics

1363. **The Clinical Pharmacology of Isosorbide Dinitrate: a Unique, New Nitrated Polyalcohol**
D. A. SHERBER and I. J. GELB. *Angiology* [*Angiology*] **12**, 244–248, June, 1961. 2 figs., 12 refs.

The authors of this paper from Fordham and Mount Sinai Hospitals, New York, describe the results obtained with isosorbide dinitrate in angina pectoris in 119 patients (81 male and 38 female). Of these, 108 received the drug after treatment with pentaerythritol tetranitrate had proved ineffective. Initially isosorbide was given in a dosage of 5 mg. 4 times a day before meals and at bedtime; after one week the dosage was increased to 10 mg. at the same intervals. The purpose of the smaller initial dose was to reduce the incidence and severity of the temporary vascular headache, to which tolerance developed. Some patients required larger doses, and in some the severity of the headache necessitated administration of salicylates. There was almost complete relief of angina in 89 patients; of the remaining 30, 24 had fewer attacks although they still required nitroglycerin occasionally. Continued treatment was refused by 4 patients because of headache; only one [*sic*] patient had no relief. The authors consider isosorbide dinitrate to be the most effective long-acting coronary vasodilator available and, given sublingually, to be superior to nitroglycerin because its action lasts for 2 to 3 hours.

A. Schott

1364. **A Possible Application of Vasodilatators in Acute Coronary Occlusion**
R. N. HEDGES JR., W. SCHMIDTKE, and R. E. LESLIE. *Angiology* [*Angiology*] **12**, 249–253, June, 1961. 19 refs.

Working at the University of Illinois College of Medicine and the Presbyterian and St. Luke's Hospitals, Chicago, the authors have examined, experimentally and clinically, the hypothesis that administration of a coronary vasodilator may be advisable in acute coronary occlusion, using for this purpose isosorbide dinitrate. Of 17 dogs (including 3 controls) all of which were subjected to ligation of the circumflex branch of the left coronary artery, one group of 7 received an intravenous infusion of 500 ml. of 5% dextrose in water with 2 g. of calcium gluconate over one hour before ligation; 20 minutes before ligation one g. of magnesium sulphate, one unit of insulin per kg. body weight (to prevent ventricular fibrillation), and 0·1 mg. per kg. of isosorbide dinitrate were given in succession intravenously. Another group of 7 animals were given the same amount of isosorbide dinitrate only. In the surviving dogs in both groups the same amount of isosorbide dinitrate was given again one hour after ligation. The 3 control dogs died within 30 minutes of operation from ventricular fibrillation. In each of the treated groups 3 dogs survived more than 3 days.

Isosorbide dinitrate in a dosage of 10 mg. 4 times a day was substituted for papaverine in 32 patients with acute myocardial infarction and was well tolerated. The authors state that this work is preliminary and that "further evaluations will be needed before the exact therapeutic potential of these methods can be assessed".

A. Schott

1365. **The Effects of Isosorbide Dinitrate on Coronary Vascular Resistance**
J. P. BUCKLEY, M. D. G. ACETO, and W. J. KINNARD. *Angiology* [*Angiology*] **12**, 259–263, June, 1961. 12 refs.

The effect of isosorbide dinitrate and pentaerythritol tetranitrate on coronary vascular resistance in anaesthetized dogs was studied at the University of Pittsburgh, Pennsylvania, the resistance being calculated from the following formula:

$$\frac{\text{Mean blood pressure (mm. Hg)}}{\text{Mean coronary flow (ml. per minute)}}$$

The drugs were administered intravenously and intraduodenally in dosages of 0·5, 0·25, and 0·1 mg. per kg. body weight.

Both drugs decreased coronary vascular resistance. Statistical analysis showed that isosorbide dinitrate given intraduodenally in tablet form was more effective in reducing coronary vascular resistance than pentaerythritol. It produced coronary vasodilatation, as evidenced by the observation that coronary blood flow was usually maintained at a rate close to the previous level in spite of a marked fall in arterial blood pressure.

A. Schott

1366. **Antiheparin and Hemagglutinating Activities of Polybrene**
P. LALEZARI and T. H. SPAET. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **57**, 868–873, June, 1961. 2 figs., 9 refs.

Hexadimethrine bromide ("polybrene"), a synthetic polymer, the molecular weight of which can be varied, has recently been used for the neutralization of heparin. At Montefiore Hospital, New York, the agglutination of human erythrocytes and platelets by hexadimethrine with a molecular weight of 6,000 was studied and compared with that of the compound with a molecular weight of 2,000.

The commercially available preparation of hexadimethrine bromide (molecular weight 6,000) was found to be an antagonist of heparin, but if used in excess was an anticoagulant. Human erythrocytes and platelets became strongly agglutinated. This agglutination of erythrocytes was reversed by the addition of heparin, but not the agglutination of platelets. The compound with the smaller molecular weight was found to have neither an agglutinating nor a significant anticoagulant effect, while it was still a potent heparin neutralizer. It is suggested that the agglutination may be the result of "neutralization of cell charge and binding of cells by the long-chain polymer".

A. S. Douglas

Chemotherapy

1367. **Specificity of Interferon**
R. D. ANDREWS. *British Medical Journal* [*Brit. med. J.*] 1, 1728–1730, June 17, 1961. 2 figs., 12 refs.

Interferon is a wide-range antiviral substance developed by interaction between living cells and live or killed virus. Particular interest attaches to its potential therapeutic value in virus diseases of man and animals. The present investigation was undertaken at Glaxo Laboratories, Greenford, Middlesex. Samples of interferon were prepared in cell cultures of different animal species (rabbit kidney, cynomolgus or rhesus monkey kidney, and human amnion), and in chick chorio-allantoic membranes by interaction with inactivated influenza virus. Laboratory procedures relating to the preparation of interferon and control fluids (cultures uninfected with virus) and to the concentration of certain samples are described. The antiviral activity of the interferon samples was compared, using vaccinia as the test virus, in intradermal tests on the rabbit and monkey.

Three experiments, each using 6 rabbits, were performed in which each rabbit was injected intradermally at each of 10 to 12 sites with 0·1 ml. of interferon or control fluid and 0·1 ml. of vaccinia virus was injected at each site, either immediately or 24 hours afterwards. In addition, groups of 6 rabbits were injected with control fluids followed by vaccinia virus. When the injection of interferon preceded that of virus by 24 hours the development of necrotic vaccinial lesions (which occurred in 4 to 6 out of 6 controls) was entirely suppressed not only by the homologous rabbit interferon, but also by 5 heterologous interferons (1 cynomolgus and 1 rhesus monkey, 1 human, and 2 concentrated chick); further, the mean diameter of the erythematous reaction was considerably reduced. Three further heterologous interferons (1 cynomolgus and 2 chick) exhibited antiviral activity, but in lesser degree. When interferon and virus were injected at the same time the homologous rabbit interferon was again effective in entirely suppressing vaccinial necrosis; so also, in all but one animal, was one heterologous interferon (cynomolgous monkey). Lesser and varying degrees of activity were shown by 3 among 5 further heterologous interferons.

Tests were similarly performed on one cynomolgus monkey into which virus was injected intradermally 24 hours after interferon samples or control fluid. Suppression of vaccinial necrosis and erythema was effected by the homologous cynomolgus monkey interferon and also by 1 heterologous interferon (chick, concentrated by freeze-drying). Rhesus monkey interferon gave some, though lesser, protection. Two further heterologous interferons (1 chick and 1 rabbit, both concentrated by dialysis) were ineffective.

The finding that interferon prepared in cell cultures of one animal species can show marked activity *in vivo* against virus infection in another animal species has a bearing upon the production of interferon for human use. It indicates that cultures of cells other than human may be utilizable for this purpose. *Joyce Wright*

1368. **Experiences with Furaltadone in a Chronic Disease Hospital**
S. ROSENFELD, D. LEICHTER, and M. G. GOLDNER. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] 9, 651–654, Aug., 1961. 3 refs.

The value of a synthetic antibacterial agent, furaltadone, in the treatment of severe or resistant infections of the skin, lungs, and kidneys was assessed in 60 patients at the Jewish Chronic Diseases Hospital, New York. Bacteriological examination of cultures in 47 cases revealed that in 36 the causative organism was *Staphylococcus aureus*. The drug was given by mouth in a dosage of 250 mg. 4 times daily for 2 to 25 days (average 6 days). There was clinical and bacteriological cure in 42 cases and improvement in 6; the results were inconclusive in 6 and in the remaining 6 (including 3 fatal cases) treatment was a failure. Gastro-intestinal disturbance and pruritus occurred in 4 patients, necessitating withdrawal of the drug. No toxic effects on the blood or nervous system were observed.

The factors leading to infection in hospitals for chronic diseases are discussed, including advanced age and poor resistance of the patients, diabetes, inadequate antiseptic measures, malnutrition, and the chronic diseases themselves. The urgent need for new and safer drugs in the treatment of infections not responding to conventional measures in hospitals for chronic diseases is emphasized and it is concluded that furaltadone is an effective agent for this purpose. *Gerald Sandler*

1369. **Furaltadone: Antibacterial Activity *in vitro* and in Serum of Patients during Treatment**
C. G. MCCARTHY and M. FINLAND. *Archives of Internal Medicine* [*Arch. intern. Med.*] **107**, 863–871, June, 1961. 19 refs.

Reports on the use of the nitrofuran derivative furaltadone (" altarfur ") as a chemotherapeutic agent for staphylococcal and other infections have ranged from the enthusiastic to the completely sceptical, and various serious side-effects involving the cardiovascular and nervous systems have also been reported. The present study, from Boston City Hospital and Harvard Medical School, is an attempt at critical evaluation of the place of furaltadone in clinical practice.

Bacteriological studies *in vitro* showed that the drug inhibited the growth of Gram-positive and Gram-negative cocci and other organisms. Following these experiments 9 patients with severe infections were treated with intravenous injections of furaltadone, from which none of them benefited; specimens of their serum, urine, and bile showed no antibacterial action which

could not be accounted for by previously administered antibiotics. Similarly, 95 specimens of serum from 12 patients treated postoperatively with furaltadone were completely lacking in antibacterial activity against the test staphylococci, and 3 of the 12 patients developed postoperative infections despite the furaltadone therapy. Dilution of the drug in serum or urine *in vitro* did, however, yield antibacterial activity [suggesting that furaltadone is inactivated before it reaches the plasma or other body fluids].

It is concluded that furaltadone cannot be expected to influence severe infections, as has been claimed.

T. B. Begg

1370. **Relative Antimicrobial Activity of Topical Chemotherapeutic Compounds when Tested, *in vitro*, in the Presence and Absence of Human Serum**

W. I. METZGER and C. J. JENKINS JR. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **11**, 335–339, May [received July], 1961. 18 refs.

At Cook County Hospital, Chicago, the minimum inhibitory concentration of dequalinium chloride (a salt of decamethylene bis-4-aminoquinaldinium) for recently isolated strains of a β-haemolytic *Streptococcus*, *Staphylococcus aureus*, a strain of *Klebsiella*, and *Candida albicans* was determined *in vitro* both in the presence and the absence of 20% human serum. The activity of the drug was compared with that of 8 other antimicrobial compounds, which included a phenol derivative, a flavine derivative, a mercury salt, and several surface active agents. All the compounds had marked antimicrobial activity in the absence of serum, but their activity, except that of dequalinium chloride, was decreased by the presence of serum, in some cases by as much as 128-fold. It is suggested that dequalinium chloride should be of value in the suppression and treatment of infections of the skin due to invasion by the organisms investigated.

Janice Taverne

1371. **Tylosin, a New Antibiotic: I. Microbiological Studies**

J. M. MCGUIRE, W. S. BONIECE, C. E. HIGGENS, M. M. HOEHN, W. M. STARK, J. WESTHEAD, and R. N. WOLFE. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **11**, 320–327, May [received July], 1961. 3 refs.

Tylosin, a new antibiotic substance, has been obtained from soil isolates tentatively identified as strains of *Streptomyces fradiae* (Waksman and Curtis) Waksman and Henrici. Tylosin is markedly active *in vitro* against Gram-positive bacteria, certain Gram-negative bacteria, and mycobacteria. It is well tolerated in animals, and is effective in experimental mouse infections against Gram-positive bacteria, *Hemophilus influenzae*, and meningopneumonitis virus. Administered parenterally, tylosin is moderately effective against tuberculosis in mice, but it does not protect against infections with influenza PR8A and murine encephalomyelitis viruses. The pattern of induced resistance in *Staphylococcus aureus* is similar to that with penicillin and erythromycin. Partial cross resistance with erythromycin is found, but no cross resistance with penicillin or the tetracyclines has been demonstrated.—[Authors' summary.]

1372. **Tylosin, a New Antibiotic: II. Isolation, Properties, and Preparation of Desmycosin, a Microbiologically Active Degradation Product**

R. L. HAMILL, M. E. HANEY JR., M. STAMPER, and P. F. WILEY. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **11**, 328–334, May [received July], 1961. 1 fig., 7 refs.

The isolation and properties of tylosin, a new antibiotic, are described. The crystalline preparation has been shown to be a pure, single component substance having the empirical formula $C_{45}H_{77}NO_{17}$. Tylosin, a weak base, forms water-soluble salts and can be acylated to form esters. Mild acid hydrolysis of tylosin yields desmycosin, another new antibiotic, and mycarose. Further degradation yields the amino sugar, mycaminose. Tylosin and desmycosin appear to belong to the macrolide class of antibiotics.—[Authors' summary.]

1373. **Antibacterial Action of Penicillin in Combination with Serum Globulins: *in vitro* Evaluation**

M. BRINGHURST and S. MARCUS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **57**, 874–882, June, 1961. 21 refs.

At the University of Utah, Salt Lake City, the effect of serum proteins upon sensitivity to penicillin was studied for three strains of *Staphylococcus aureus*, classified as highly sensitive, moderately sensitive, and resistant to penicillin. Gamma globulin markedly increased the antibacterial activity of penicillin, the effect being proportional to the concentration of the protein. When gamma globulin was present in the same concentration as in normal serum the antibacterial activity of penicillin was increased approximately 35 times for all three strains. Normal serum displayed an activity comparable with its gamma-globulin content and albumin was without effect upon the results of the assay. Similar results were obtained by tube or disk assay and it is suggested that the method may provide better evaluation of sensitivity to penicillin for clinical purposes. *F. W. Chattaway*

1374. **Microbiological Studies on a New Broad-spectrum Penicillin, " Penbritin "**

G. N. ROLINSON and S. STEVENS. *British Medical Journal* [*Brit. med. J.*] **2**, 191–196, July 22, 1961. 5 figs., 4 refs.

The authors report the results of microbiological studies of " penbritin " (B.R.L. 1341), a new penicillin prepared from 6-aminopenicillanic acid which is acid-stable, active against a wide range of Gram-positive and Gram-negative bacteria, and highly bactericidal. The compound is 6[D(-)α-aminophenylacetamido] penicillanic acid and is sparingly soluble in water.

Studies *in vitro* showed that penbritin was only slightly less active against the pyogenic cocci than benzylpenicillin (G) and substantially more active than tetracycline and chloramphenicol. Against Gram-negative bacilli penbritin showed a range of activity generally similar to that of tetracycline. It was highly active against *Haemophilus influenzae*, *Neisseria catarrhalis*, and various members of the *Salmonella* group, but showed little activity against *Aerobacter aerogenes* and *Pseudomonas pyocyanea*.

Some strains of *Proteus* which were sensitive to tetracycline were resistant to penbritin, but in 82% of 121 strains tested the minimum inhibitory concentration (M.I.C.) was 5 μg. per ml. or less. Penbritin is not stable to penicillinase and therefore was not effective against penicillinase-producing organisms. The presence of serum had little effect on M.I.C. values, nor had the size of the inoculum in tests with *Salm. typhi* or *Shigella sonnei*. In most tests the *p*H had no significant effect on the activity of penbritin, but against two strains of *Escherichia coli* and one of *Streptococcus faecalis* the antibiotic was more active at a slightly acid *p*H than at higher *p*H values. Emergence of strains resistant to penbritin developed stepwise in the typical penicillin manner. *A. Ackroyd*

1375. **"Penbritin"—a New Broad-spectrum Antibiotic: Preliminary Pharmacology and Chemotherapy**
D. M. Brown and P. Acred. *British Medical Journal* [*Brit. med. J.*] **2**, 197–198, July 22, 1961. 1 fig., 2 refs.

In these pharmacological studies of the new broad-spectrum antibiotic "penbritin" [see Abstract 1374] it was shown that when administered in single doses of up to 5 g. per kg. body weight orally or subcutaneously, or 2 g. per kg. intravenously, or in dosages of 500 and 100 mg. per kg. daily over a period of 12 weeks penbritin was non-toxic to rats and mice, causing no arrest of growth and no biochemical, haematological, or histological abnormalities. In dogs, penbritin was better absorbed and gave more prolonged blood levels than phenoxymethylpenicillin or phenethicillin. It was shown to be evenly distributed throughout the body tissues apart from the kidneys and liver, in which concentrations higher than those in the serum were demonstrated. The antibiotic is excreted in the urine and bile and was found in considerable concentrations in these fluids. In mice its effectiveness against infections due to *Staphylococcus aureus* or *Streptococcus pyogenes* (Group A) was equal to that of the existing oral penicillins, while against infections due to *Salmonella typhimurium* or *Klebsiella pneumoniae* its activity appeared to be greater than that of tetracycline or chloramphenicol. This was in marked contrast to the titres obtained *in vitro*, in which only small differences were found. *A. Ackroyd*

1376. **Absorption and Excretion of "Penbritin"**
E. T. Knudsen, G. N. Rolinson, and S. Stevens. *British Medical Journal* [*Brit. med. J.*] **2**, 198–200, July 22, 1961. 2 figs.

The authors have determined the serum concentrations and urinary excretions occurring in 17 normal human subjects after various oral doses of "penbritin". The antibiotic was well tolerated and absorbed, peak serum concentrations varying from 2·19 μg. per ml. after a dose of 250 mg. to 6·79 μg per ml. after one of 1,000 mg. being generally obtained about 2 hours after administration, compared with ½ to 1 hour after other acid stable penicillins, and significant serum concentrations were still present at 6 hours, while doubling the dose virtually doubled the peak serum concentration. Some 30% of a given dose was excreted in the urine over a 6-hour period. In 4 subjects who were given 500 mg. every 8 hours for 4 days there was no accumulation of penbritin in the serum, the levels obtained on the 4th day being, on the whole, lower than those on the first.

For therapeutic trials the authors recommend that 250 mg. should be given 6 hourly for the treatment of infections due to Gram-positive organisms or to *Haemophilus influenzae*, a dosage of 250 to 500 mg. every 6 or 8 hours for urinary infections in view of the high concentration obtained in the urine, and 750 mg. or more 8-hourly for the majority of infections due to Gram-negative organisms. *A. Ackroyd*

1377. **"Penbritin": an Oral Penicillin with Broad-spectrum Activity**
G. T. Stewart, H. M. T. Coles, H. H. Nixon, and R. J. Holt. *British Medical Journal* [*Brit. med. J.*] **2**, 200–206, July 22, 1961. 3 figs., 11 refs.

The authors report the results of microbiological and clinical studies with the new oral penicillin "penbritin". The results of the former studies, while in general similar to those reported by Rolinson and Stevens [see Abstract 1374] showed a few comparatively minor differences. Whereas penbritin was active against many coliform organisms, the majority of strains of *Escherichia coli* were inhibited only by higher concentrations (5 to 50 μg. per ml.), at which even benzylpenicillin began to be effective. Organisms such as *Aerobacter aerogenes*, *Proteus morganii* and *Pseudomonas pyocyanea* were uniformly resistant. In tests with *Staphylococcus aureus* the minimum inhibitory concentration was shown to be dependent on the size of the inoculum, but this was not the case with sensitive coliforms. Generally, Gram-negative organisms which were resistant to a concentration of 10 μg. per ml. or more were resistant to other forms of penicillin at this concentration, although there were some exceptions. Cross-resistance of *Staph. aureus* was also not invariable. In a trial at Queen Mary's Hospital for Children, Carshalton, Surrey, on 8 selected children with well-established refractory urinary infections due to sensitive coliforms and/or streptococci of Group D, 10 children with other infections, including one child with peritonitis due to *Salmonella typhimurium*, and another with meningitis due to streptococci in whom penbritin was injected intraventricularly in a dosage of 2 to 4 mg. daily for 4 days, rapid responses occurred to a 5-day course of 50 to 100 mg. per kg. body weight daily, but in 6 alimentary carriers of *Salm. typhimurium* and 2 of *E. coli* serotypes the infections were not cleared. Suppression of the faecal flora lasted until about 48 hours after the last dose.

Assay of serum or plasma showed that inhibitory levels (0·5 to 5 μg. per ml.) were attained and maintained for between 1½ and 7 hours after oral doses of 50 to 100 mg. per kg. per day. Assay of urine showed concentrations greatly in excess of those required for the inhibition of sensitive organisms (500 to 4,000 μg. per ml.). Excretion began within 3 hours, increased steeply during the next 3 or 4 hours, continued for 12 hours after the last dose, and ceased after 48 hours. Toxic effects were minimal and transient. *A. Ackroyd*

Infectious Diseases

1378. **An Epidemiological and Clinical Description of an Epidemic Outbreak Caused by E.C.H.O. 7 Virus.** (Эпидемиологическое и клиническое описание вспышки заболеваний, вызванных вирусом ECHO 7) I. V. Šarlaj, M. A. Morozenko, and R. A. Grinval'd. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **6**, 57–61, July, 1961. 2 refs.

The large group of E.C.H.O. viruses includes 24 types, of which 10 have been found in cases of serous meningitis, while 5 others have been responsible for epidemics of enteritis and one (Type 8) for catarrh and otitis. Type 7 is usually regarded as of low morbidity, but Henigst working in Munich isolated it in 119 children during an epidemic of upper respiratory catarrh (*Dtsch. med. Wschr.*, 1959, **84**, 1022).

The present authors describe an epidemic in the creches of Leningrad involving 11 out of 16 children ranging in age from 18 months to 2 years in which E.C.H.O. Type 7 was isolated. The symptoms were 1 to 3 days' pyrexia, catarrh, antero-cervical lymphadenitis, and enlargement of the liver and spleen. The lymph nodes, liver, and spleen remained palpable for 2 to 3 weeks. One child developed bronchopneumonia; from this case a haemolytic staphylococcus was isolated which was insensitive to penicillin, streptomycin, biomycin, and levomycetin (" aureomycin "; chlortetracycline). This child made a good recovery and was discharged on the 25th day from onset. The incubation period varied from 8 to 14 days. The results of liver function tests were normal, except that for thymol turbidity, which was raised in 5 cases. The virus was isolated from the faucial discharge and the stools. Immunological tests showed a raised titre to E.C.H.O. Type 7 virus in 6 cases, both to standard strains and to others obtained from patients, but not to other virus strains, including influenza Types A, A1, B, and C, para-influenza virus Types AA1, AA2, CA, and all other E.C.H.O. types. There seems no doubt that E.C.H.O. virus Type 7 was the pathogenic organism responsible for the outbreak. *L. Firman-Edwards*

1379. **Outbreak of E.C.H.O. Type 9 Infection in a Children's Home**
F. L. Constable and L. F. Howitt. *British Medical Journal* [*Brit. med. J.*] **1**, 1483–1486, May 27, 1961. 1 fig., 5 refs.

An outbreak of infection due to E.C.H.O. virus Type 9 occurred in a residential children's home in Edinburgh in 1960. Within a period of 16 days, 19 out of the 27 children and 10 adults connected with the home showed clinical signs of infection, 13 of them within a period of 6 days. Abdominal pain was the most frequent presenting symptom, followed by headache, alone or accompanied by abdominal pain. A rash developed in one child only, the rash being blotchy in character and occurring on the face, neck and trunk. The duration of pyrexia ranged from 2 to 6 days, although in 2 children the course of the illness was biphasic. E.C.H.O. virus Type 9 was isolated from the faeces of 12 of the 19 affected subjects. Specimens of serum from 14 cases were examined, and all showed high or rising titres of neutralizing antibody to the virus. Suckling mice were inoculated intracerebrally with faecal specimens which had proved negative on tissue culture inoculation, but no virus was isolated by this procedure.
J. E. M. Whitehead

1380. **Mumps Epididymo-orchitis and Its Treatment with Cortisone: Report of a Controlled Trial**
R. S. Kocen and E. Critchley. *British Medical Journal* [*Brit. med. J.*] **2**, 20–24, July 1, 1961. 2 figs., 17 refs.

A mumps epidemic affecting nearly 300 patients occurred among Gurkha recruits arriving in Malaya between December, 1959, and February, 1960, and in 35 of them epididymo-orchitis developed. All 35 patients were admitted to the British Military Hospital, Taiping, and treated with rest in bed and analgesics, 18 of them, selected at random, being also given a 6-day course of cortisone, totalling 950 mg., by mouth. Clinical observations were strictly controlled, and after discharge from hospital patients seen again at approximately 3, 5, and 7 months. In the cortisone-treated group the duration of pyrexia was significantly shorter than in the controls, but there was no other difference between the two groups. Testicular degeneration was found to be progressive for at least 5 months after the attack, but was uninfluenced by the corticosteroid therapy.

On the basis of this experience and a review of the literature the authors conclude that corticosteroid therapy is not effective in the treatment of mumps epididymo-orchitis. *Winston Turner*

1381. **Nasal Disinfection in Prevention of Post-operative Staphylococcal Infection of Wounds**
R. J. Henderson and R. E. O. Williams. *British Medical Journal* [*Brit. med. J.*] **2**, 330–333, Aug. 5, 1961. 7 refs.

A controlled trial of prophylactic nasal disinfection was made on 850 surgical patients, who received alternately " naseptin " cream (containing chlorhexidine hydrochloride and neomycin sulphate) and an inert base. Of the 850 patients, 66 (7·8%) developed clinical sepsis and infection; 163 (19·2%) were clean but bacteriologically infected—that is, a clean wound yielding pathogens on swabbing; and 16 (1·9%) were septic but not infected—that is, a septic wound yielding no pathogens. The naseptin prophylaxis was directed at the *Staphylococcus aureus* only, and 47·5% of the septic cases were infected by this organism. There was no significant difference in the *Staph. aureus* sepsis rate between the

naseptin-treated group (5%) and the control group (4·6%). Of the treated group of 420 patients, 346 (82·4%) had nasal swabs free from *Staph. aureus* and only 49 (11·7%) acquired staphylococci in the ward. The corresponding figures for the 413 controls were 223 (54%) sterile and 120 (29·1%) infected. In the treated group 266 patients were persistently non-carriers, but 12 (4·6%) of these developed sepsis compared with 2 (1·1%) of 189 non-carriers among the controls. The naseptin appeared to control the nasal carriage of staphylococci, but did not reduce the sepsis rate. The authors consider that nasal colonization may be a measure of environmental staphylococcal contamination and only indirectly a cause of wound sepsis. *Winston Turner*

1382. **Self-contamination of Patients with Staphylococcal Infections**

R. HARE and E. M. COOKE. *British Medical Journal* [*Brit. med. J.*] **2**, 333–336, Aug. 5, 1961. 9 refs.

Bacterial sampling for *Staphylococcus aureus* was carried out at St. Thomas's Hospital, London, on selected areas of skin, nose, hair, and various articles of clothing and bedding, and also on the floor around the beds, of patients suffering from a variety of infective conditions caused by this organism. In patients with postoperative infection the number of organisms was not large unless there was a very profuse discharge into the dressings. All these patients were having antibiotic therapy, which by itself had not, therefore, reduced the risk of contamination. In patients with other types of lesion heavy contamination occurred only when the bacterial source was secondary infection of extensive skin lesions, pneumonia, or enterocolitis, where the lesions could not be occluded by dressings. That the contaminating organisms originated from these foci of infection was proved by phage typing. Blankets were not found to be a major vector for spread of infection. The authors consider that isolation or segregation should be reserved for patients where this type of infection is most likely to occur. *Winston Turner*

1383. **Staphylococcal Septicaemia in a General Hospital**

D. E. B. POWELL. *British Medical Journal* [*Brit. med. J.*] **2**, 336–339, Aug. 5, 1961. 2 figs., 23 refs.

During the 9-year period 1950–8 in a 360-bed general hospital in Cardiff staphylococcal septicaemia occurred in 49 patients, of whom 40 died, a mortality of 82%. The condition has become more frequent since 1955. There was no difference between the sexes, and mortality did not seem to be related to age. In 37 patients there was evidence of a primary focus of infection, especially in skin, respiratory tract, central nervous system, or bones. In the last group all 3 patients with acute osteomyelitis recovered. Evidence of non-suppurative renal lesions was frequently present, and all patients with a blood urea level exceeding 100 mg. per 100 ml. died. The infection was postoperative in 9 patients, of whom 8 died. In 7 cases the infection occurred during the course of steroid therapy and all were fatal. The non-fatal cases had a history of a few days' duration only, whereas all patients with a history of more than 21 days died. The highest mortality (94%) occurred in those patients who contracted the infection while in hospital, and this in spite of liberal antibiotic therapy.

Winston Turner

1384. **The Complications of Typhoid Fever**

H. A. K. ROWLAND. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **64**, 143–152, June, 1961. 15 refs.

This is a useful record of the complications of typhoid fever found in a large series of cases (530) treated with chloramphenicol at the National Iranian Oil Company Hospital, Abadan. Some received prednisolone in addition, but this had practically no effect other than a more rapid reduction of pyrexia. In assessing the overall effect of chloramphenicol treatment the author compares his results with some of those reported in pre-chloramphenicol days as well as with other series treated with chloramphenicol. [He does not, however, mention the series of 876 cases (of which about two-thirds were non-European), with 80 deaths, treated in Pretoria by Nelson and Pijper (Banks, *Modern Practice in Infectious Fevers*, Butterworth, London, 1951) before the introduction of chloramphenicol; this series would seem closely to resemble his own as regards type of patient, nursing, and general care. If he had done so, however, his main conclusions would not have been invalidated but, on the whole, strengthened.]

His conclusions are that, as compared with the pre-chloramphenicol era: (1) there had been a significant decrease in mortality (from 10 to 12% to about 3·5%) and in intestinal haemorrhage [although this is doubtful, and his figure of 3·6% incidence seems worse than the South African figure of 1·6%, which excluded streaky blood in the stool without other symptoms]; (2) there has been a large decrease in total complications, especially those associated with a long debilitating illness (pneumonia, venous thrombosis, parotitis, bedsores, and secondary infections); (3) there has been no decrease in the incidence of perforation; and (4) there has been a significant rise in the relapse rate. He used chloramphenicol freely and in multiple courses at times, and from his own and other experience concludes that bone-marrow damage, if due to chloramphenicol, must be a rare event.

[Few, if any, who have had experience of the treatment of typhoid fever before and after the introduction of chloramphenicol would hesitate to use this drug.]

H. Stanley Banks

1385. **Pseudomonas Bacteremia: Review of Ninety-one Cases**

J. A. CURTIN, R. G. PETERSDORF, and I. L. BENNETT JR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **54**, 1077–1107, June, 1961. Bibliography.

In this review of the problem of pseudomonas bacteriaemia in man the records were analysed of 88 patients with 91 episodes of bacteriaemia admitted to Johns Hopkins Hospital, Baltimore, between 1940 and 1959. There were 73 deaths and post-mortem examinations were carried out in 55 cases. *Pseudomonas aeruginosa* was isolated from the blood in all 91 cases, in 68 during

life and in 23 at necropsy. The patients are considered in 4 groups—premature infants (18), children with severe congenital or acquired diseases (27), those with lymphoma or leukaemia (28), and 18 adults with a variety of chronic debilitating diseases. Pseudomonas bacteriaemia was most frequent in the very young or in those past middle age; of the 88 patients, 27 were under 6 months of age and 19 under 12 years, while 13 of the 18 adults were over 50 years (mean age 60). Males predominated, especially among the premature infants and the elderly. It was apparent that chronic disease, debility, prematurity, infancy, coexisting infections, and surgical procedures were all associated with pseudomonas infections. The prognosis was poor, there being only 15 survivors. The bacteriaemia was successfully treated in a further 12 cases, but death occurred as the result of associated disease. In general the endogenous defence mechanisms of the host were an important determinant of the outcome, while in this series the associated disease state was the most important single factor affecting the outcome.

The clinical picture was not characteristic and in the adults resembled any other type of bacteriaemia. Among the infants fever was unusual. Ecthyma gangrenosum, diagnostic of pseudomonas septicaemia, was found in only one patient. In 22 cases the pseudomonas infection occurred as a superinfection to an already existing bacteriaemia from some other organism; there were 27 bouts of mixed infection in all, staphylococci (11 cases) and enterococci (6) being the most frequently associated organisms. In adults the bacteriaemia followed operations on the urinary tract in 11 cases and in these the prognosis was much better than in the patients with debilitating conditions. Of the 88 patients, 56 developed the pseudomonas infection while receiving one or more antibiotics either prophylactically or therapeutically and it seemed likely that the infection was facilitated by alteration of the natural bacterial flora by these antibiotics. The response to treatment was very variable and depended to a great extent upon the underlying disease. Polymyxin B proved to be the most effective antibiotic, especially when given with streptomycin.

John Fry

1386. **Latent Brucellosis in Farmers**

I. McWHINNEY and A. P. PRIOR. *British Medical Journal* [*Brit. med. J.*] **2**, 80–81, July 8, 1961. 9 refs.

In the Stratford-on-Avon district, an area of mixed arable and stock farming but with no preponderance of dairy herds, evidence of brucellosis was detected in 14 out of 20 farmers examined. After a detailed inquiry for a history of any febrile illness a brucellin skin test was performed and specimens of blood were removed for agglutination tests. The brucellin test yielded positive results in 11 cases, and in this group the results were mainly strongly or very strongly positive. Brucella agglutination to a titre of at least 1 in 40 was taken as evidence of past or present latent brucellosis; a positive brucellin reaction was also considered to indicate latent infection. It is noteworthy that during a recent survey in Oxfordshire between 4·4 and 8% of farms were found to be producing brucella-infected milk.

Almost certainly 2 of the men had suffered from undiagnosed undulant fever. The first man had denied any history of a febrile illness until the general symptoms produced by a brucellin test recalled to his memory an illness experienced 10 years previously, during which he had complained of discomfort, headache, limb pains, and sweating. The man had to stop work for a few days, but the symptoms persisted for 3 months. About the year 1950 the second man had a bout of pyrexia accompanied by malaise, profuse sweating, and limb pains. There was a history of contagious abortion in his milking herd.

The authors support Dalrymple-Champney's contention that the real incidence of brucellosis is higher than the reported incidence. The diagnosis of this disease should be borne in mind whenever a farm worker is found to have pyrexia of unknown origin or symptoms such as malaise, sweating, and pains in the limbs. In this context, among patients belonging to the farming community no significance should be attached to a titre of up to 1 in 320 or a rise in titre after a positive brucellin reaction.

A. Garland

1387. **Boils and Allergy. II. Investigation of Boils in General Practice.** [In English]

B. BENDKOWSKI. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **16**, 91–120, 1961. 1 fig., bibliography.

In a general practice in Barrow in Furness 250 out of a total of 5,350 patients had various allergic diseases. Over a period of 15 months 60 patients were treated for boils and 53 of these also suffered from allergic disorders. The majority (70%) of the patients with boils were also nasal carriers of *Staphylococcus pyogenes*. Of a control series of 100 allergic patients, 65 gave a past history of boils and 71 were nasal carriers of *Staph. pyogenes*. Of a further control series of 100 non-allergic patients, only 15 remembered having had boils in the past and 44 were nasal carriers of the staphylococcus. It is suggested that "allergic diseases predispose the patients to be nasal carriers of *Staph. pyogenes*" and this gives rise to the high incidence of boils in such patients.

A. W. Frankland

1388. **Sarcoidosis Presenting with Polyarthritis**

M. J. WILLIAMS. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **20**, 138–143, June, 1961. 3 figs., 12 refs.

The author reports 7 patients (6 middle-aged women and one man) seen at Aberdeen Royal Infirmary with sarcoidosis in whom the presenting manifestation was polyarthralgia of the large limb joints. Erythema nodosum developed subsequently in 5 cases and bilateral hilar lymphadenopathy was present in 6. The erythrocyte sedimentation rate was always raised and the Rose–Waaler test gave a negative response; the antistreptolysin titre was normal in all cases. In 6 of the 7 patients a positive Kveim reaction was obtained; the patient giving a negative result was receiving prednisone at the time. In all cases symptoms subsided spontaneously, making corticosteroid therapy unnecessary.

D. Geraint James

Tuberculosis

1389. **Tuberculosis in Soho**
P. A. EMERSON, G. BEATH, and J. G. TOMKINS. *British Medical Journal* [*Brit. med. J.*] **2**, 148–152, July 15, 1961. 10 refs.

Of the 3,105 catering establishments in the City of Westminster, over 400 are concentrated in the electoral ward of Soho: 2,611 workers in 240 of these establishments were examined by interview and mass radiography and 86 showed radiological evidence of present or past tuberculosis. The 86 cases were divided into 3 groups: an active group in which there were 21, of whom 6 had a positive sputum and 15 a negative sputum; a second group containing 32 patients who, it was considered, required observation; and a third group containing 33 patients in whom it was decided the tuberculosis had been arrested. These figures indicate that the incidence of active tuberculosis was 8 per 1,000 workers radiographed. When this figure was analysed according to occupation it was found that the incidence in employers and managers was 8·6 per 1,000; in food servers 6·2; in food preparers 10·6; in other kitchen staff 13·6; and in alcohol servers 12·7.

When the figures were analysed by country of origin it was found that of the 840 workers born in Great Britain, active tuberculosis was present in 4 (4·8 per 1,000). Of the remaining 1,771, all of whom were immigrants, active tuberculosis was found in 17 (9·6 per 1,000), and when the immigrant figures were analysed it was found that the incidence among the Chinese, who had mostly come from Hong Kong, was 53·8 per 1,000. If the Chinese were excluded the incidence of active disease among the rest of the immigrants was only 4·4 per 1,000, a lower figure than for those born in Great Britain. In those cases in which a decision was possible, tuberculosis appeared to have developed more often after than before joining the trade—in workers from Great Britain (12:4); in those from Cyprus (5:2); and in those from other European countries (6:3). The disease appeared to have developed more often before than after joining the trade in those from China and Hong Kong (11:8); in those from Italy (6:2); in those from Ireland (2:1); and in those from the West Indies (1:*nil*). The incidence was the same before and after in those from India and Pakistan (2:2).

The survey therefore shows that tuberculosis is more than 4 times as common in the catering trade in Soho as in the general population of London, where the rate is 1·2 per 1,000 males and 0·7 per 1,000 females. The evidence is that more than half the tuberculous workers have the disease before joining the catering trade and the majority of these come from Hong Kong and to a lesser degree from Italy and Ireland, where there is a high national incidence of the disease. Those tuberculous workers born in Great Britain and others from areas such as Cyprus, where the incidence of tuberculosis is low, usually join the trade healthy, but may develop the disease in the first 5 years after joining the trade. The authors therefore recommend that all new entrants to the catering trade in Soho should be radiographed and tuberculin tested whether they come from abroad or are born in the United Kingdom; for those from China and Hong Kong these precautions are especially necessary.

Kenneth M. A. Perry

1390. **Tobacco, Alcohol and Tuberculosis**
K. E. BROWN and A. H. CAMPBELL. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **55**, 150–158, July, 1961. 1 fig., 11 refs.

On examining [at the Macleod Repatriation Sanatorium, Victoria, Australia] the tobacco and alcohol consumption of 100 tuberculous patients before diagnosis and of controls, it was found that tuberculous patients were excessively heavy consumers of alcohol and to a lesser extent of tobacco. The tuberculous patients averaged the equivalent of nine 7-ounce [199-ml.] glasses of beer daily compared with three glasses by the controls. The difference between the two groups is statistically highly significant ($t=6{\cdot}65$, $P<0{\cdot}001$). Heavy smoking and heavy drinking were found to be linked together independently of tuberculosis. When the alcohol consumption of the tuberculous group and the controls was matched there was no difference between the smoking habits. In contrast, alcohol consumption was found to remain excessive when the smoking habits were matched. Thus, of the two habits, alcohol and not smoking was more directly associated with tuberculosis. The incidence of tuberculosis appeared to increase with the amount of alcohol consumed.

Although the present investigation cannot be regarded as proving that the relationship between alcohol and tuberculosis is causal, the results indicate that case-finding amongst heavy drinkers would be profitable and suggest the need for further investigation of the effect of the drinking habits of a community upon the incidence of tuberculosis.—[From the authors' summary.]

1391. **Viral Influenza and Pulmonary Tuberculosis.** (Virusgrippe und Lungentuberkulose)
H. HOFFMANN and E. J. FISCHER. *Münchener medizinische Wochenschrift* [*Münch. med. Wschr.*] **103**, 1181–1184, June 9, 1961. 3 figs., 4 refs.

In this study of the part played by viral influenza in both the pathogenesis and reactivation of pulmonary tuberculosis 415 patients were examined at the University Medical Clinic, Bonn, during the years 1954 to 1957. The diagnosis of a viral influenza infection was based on the clinical signs and symptoms and the result of the complement fixation test. In 108 cases in which the influenza started with coryza, conjunctivitis, and redness of the mucous membranes the patients had to be ad-

mitted to hospital 6 to 8 weeks later, where their illness was then diagnosed as pulmonary tuberculosis. During the influenza epidemic of 1955 and the first half of 1956 more patients suffered from an acute form of pulmonary tuberculosis than in the second half of 1956 and 1957. In 72 patients who contracted influenza due to virus A or B the titre in the complement fixation test decreased, but the pulmonary tuberculosis persisted. It is concluded that the viral infection reduced the patient's resistance and so prepared the way for the development or reactivation of pulmonary tuberculosis.

Franz Heimann

1392. **Chemotherapy of Pulmonary Tuberculosis with Neotebanyl.** [In English]
K. A. JENSEN, P. MØRCH, and K. TØRNING. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **40**, 195–201, 1961. 4 figs., 2 refs.

There is little doubt that many tuberculous patients do not take their drugs regularly, especially the *p*-aminosalicylic acid (PAS) compounds; this can be proved by urinary examinations and may be the cause of the development of drug resistance.

The present authors, at Oeresundshospitalet, Copenhagen, have previously used a drug called "tebanyl" (or "tebamin"), which is the phenyl ester of *p*-aminosalicylic acid, in the treatment of tuberculosis, and the gastric upset with this compound has been far less than with PAS. During the past 3 years they have employed a preparation called "neotebanyl" (3 parts of tebanyl and one part of PAS), with which they claim that gastric disturbance is rare. Even so, of 69 patients given this preparation, 13 (19%) had gastric troubles severe enough to necessitate suspension of the treatment, the usual symptoms being distension and anorexia.

The authors consider that neotebanyl has a place in the long-term treatment of tuberculous patients, especially those who experience gastric upsets when taking the usual PAS preparations. *Paul B. Woolley*

1393. **Late Results of Thoracoplasties in Combination with Chemotherapy in the Treatment of Tuberculosis: a 5–7 Year Follow-up Study.** [In English]
J. E. SJÖBERG and E. TIVENIUS. *Acta tuberculosea Scandinavica* [*Acta tuberc. scand.*] **40**, 202–214, 1961. 2 figs., 34 refs.

The authors of this paper from the Renström Hospital, Göteborg, Sweden, stress the difficulty experienced in deciding, on radiological grounds, whether a tuberculous lesion is active or not after a thoracoplasty operation. Sputum conversion, they contend, is therefore of paramount importance; this may not occur until several months after thoracoplasty, but this delay does not necessarily affect the prognosis adversely. The smaller the lesion and the longer the sputum has been negative, the better is the eventual prognosis.

They report on a series of 85 tuberculous patients who received adequate chemotherapy followed by a small, limited thoracoplasty of 5 ribs. Deformity was negligible, and 5 to 7 years after the operation the disease was considered to have been arrested in 82 of the cases (6, however, had to have a resection). The operative mortality for the thoracoplasty was 1·2%. On the basis of these results the authors consider that thoracoplasty still has a place in the surgical treatment of pulmonary tuberculosis. *Paul B. Woolley*

1394. **Bronchoscopy following Pulmonary Resection for Tuberculosis.** (Бронхоскопия у больных туберкулезом после резекции легкого)
G. B. PODGAECKIJ. *Проблемы Туберкулеза* [*Probl. Tuberk.*] **39**, 40–44, No. 3, 1961. 6 refs.

Bronchoscopy was carried out postoperatively on 41 tuberculous patients, of whom 17 had been subjected to pneumonectomy and 24 to lobectomy; the disease was fibro-cavernous in 33 cases, disseminated in 3, infiltrative in one, and focal in 4. The indications for bronchoscopy were haemoptysis, dyspnoea, troublesome cough, excessive sputum, or suspected bronchial fistula. Whenever any abnormality in the bronchial mucous membrane was revealed bronchoscopy was repeated as a therapeutic measure, so that it was carried out once in 16 cases, twice in 17, three times in 3, four times in 3, and 6 times in 2, usually between 7 and 24 months after the operation. At different times between 5 and 12 months postoperatively 4 patients coughed up silk ligatures, while at bronchoscopy 3 ligatures were removed in each of 2 patients, 2 ligatures in each of 3, and 3 ligatures in one patient who had undergone resection of the right upper lobe.

Bronchoscopic examination revealed the following changes in the mucous membrane of the bronchial stump: infiltration in 10 cases, infiltration and tuberculous granuloma in 4, granulation tissue in 4, ulceration in 4, scarring in 12, bronchial fistula in 7, dilatation of the main bronchus in 13, and displacement of the trachea in 24. Tuberculosis of the bronchial stump was observed mainly in patients with pre-existing tuberculous endobronchitis. Mucosal infiltration of the bronchi on the unoperated side was demonstrated in 15 cases. Preoperative preparation of the patients greatly reduced the incidence of bronchial mucosal lesions. The treatment consisted in the removal of ligatures, excision of granuloma, painting with adrenaline, atropine, or silver nitrate, the use of aerosols, and the intratracheal administration of antituberculous drugs. *S. W. Waydenfeld*

1395. **Tuberculous Peritonitis**
F. F. JOHNSTON and J. P. SANFORD. *Annals of Internal Medicine* [*Ann. intern. Med.*] **54**, 1125–1133, June, 1961. 26 refs.

A review of the records of the Parkland Memorial Hospital, Dallas, Texas, employing strict bacteriological criteria, revealed 12 cases of proved tuberculous peritonitis occurring between 1943 and 1960, 11 of the patients being negroes and 8 of them women. Among the salient clinical features described, ascites was present in 8 cases, and signs of hepatic cirrhosis in 2. Of 9 patients subjected to skin tests, 4 had given a negative tuberculin reaction, only 2 of these being severely ill. The authors attribute this finding to transient hyposensitization of a tuberculin-sensitive individual. *B. Golberg*

Tropical Medicine

1396. **O'Nyong-nyong Fever: an Epidemic Virus Disease in East Africa. III. Some Clinical and Epidemiological Observations in the Northern Province of Uganda**
H. SHORE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] 55, 361–373, July, 1961. 2 figs., 5 refs.

The description of o'nyong nyong fever, a hitherto unknown dengue-like virus disease, presented in this paper from the Uganda Medical Service is based on the records of 49 in-patients and 704 out-patients with the disease, together with the results of 36 surveys involving no fewer than 44,326 persons. The typical syndrome consisted of joint pains, rash, and lymphadenitis. The joint pain in the knees, elbows, wrists, fingers, and ankles, appearing in that order, varied from severe pain to mild weakness. The rash usually appeared on the 4th day, lasted for 4 to 7 days, and was indistinguishable from that of measles. The lymphadenopathy affected mainly the posterior cervical group of nodes, but axillary and inguinal lymph nodes were sometimes involved. The blood picture showed a neutropenia and a relative lymphocytosis; the cerebrospinal fluid was under pressure but otherwise normal. All the patients recovered.

The epidemic appears to have started in the Obong area of the Albert Nile and the epidemiological factors are fully discussed. It appeared that previous epidemics may have left some residual immunity among persons in the older age groups.

[The clinical picture resembles that of *fièvre rouge congolaise* reported from the Congo.]

Clement C. Chesterman

1397. **Antibiotic Treatment of Acute Brucellosis Caused by *Brucella melitensis***
Z. FARID, A. MIALE JR., M. S. OMAR, and P. F. D. VAN PEENEN. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **64**, 157–163, July, 1961. 1 fig., 23 refs.

The object of this well-documented study from a U.S. Naval Research Unit based on Cairo was to determine the most effective antibiotic treatment of acute brucellosis —a disease notorious for post-treatment relapses. In all, 94 patients (all but 5 of them males) were treated for acute or subacute *Brucella melitensis* infection with one of the following three antibiotic regimens for 21 days: (1) 53 were given a combination of erythromycin, 1 g. 6-hourly, together with streptomycin and dihydrostreptomycin in alternate doses of 0·5 g. intramuscularly every 12 hours; (2) 21 patients received a combination of tetracycline, 0·5 g. 6-hourly, and the above dosage of streptomycin and dihydrostreptomycin; and (3) 20 patients were treated with tetracycline alone in a dosage of 1 g. 6-hourly. The immediate results with all 3 regimens were excellent. All the patients became afebrile and completely asymptomatic within 2 weeks of the start of therapy. Relapse rates in the three groups ranged from 10 to 14%, but all relapses cleared with further treatment, tetracycline alone being apparently fully effective for dealing with relapses. Follow-up studies at 4 to 6 weeks' interval were carried out for periods of up to 5 years.

There was thus no significant difference in the results in the 3 groups and minimal relapse rates were secured in all. It would seem that tetracycline alone in a daily dosage of 3 to 4 g. for an adult is at present the treatment of choice for acute *Br. melitensis* infection. As Spink (*J. Amer. med. Ass.*, 1960, **172**, 697) has shown, however, streptomycin may be a valuable adjunct in the treatment of acute infections due to *Br. suis* and *Br. abortus*. No evidence of chronic brucellosis was found in these patients, nor is this condition known in Egypt. [Presumably it is a rare accompaniment of *Br. melitensis* infection.] Agglutination titres were raised in every case before treatment and gradually decreased to insignificant levels following therapy. It is noted that a persistently elevated titre, or a rise after treatment, may augur a relapse.

H. Stanley Banks

1398. **An Evaluation of Intestinal Fluids in the Pathogenesis of Cholera**
R. FRETER, H. L. SMITH JR., and F. J. SWEENEY JR. *Journal of Infectious Diseases* [*J. infect. Dis.*] **109**, 35–42, July–Aug., 1961. 2 figs., 19 refs.

An evaluation of intestinal fluids in the pathogenesis of cholera was undertaken during an outbreak of the disease in Saigon in 1959 in an attempt to determine the exact site of multiplication and the pathogenic effect of *Vibrio cholerae*. It was found that the intestinal fluids were not a good medium for growth and that the severity of cholera in any case was not related to the number of vibrios in the stools. Nor did endotoxin levels, as determined by intraperitoneal injection in white mice, suggest that lysis was taking place in these fluids. Moreover, vibrio mucinase was not detectable in fluid cholera stools. It is concluded therefore that submucous penetration does not occur to any great degree and that growth on the surface of the villi in the early stages of the disease produces exogens and toxic substances responsible for the pathology.

Clement C. Chesterman

1399. **Malaria in African Children with Deficient Erythrocyte Glucose-6-phosphate Dehydrogenase**
A. C. ALLISON and D. F. CLYDE. *British Medical Journal* [*Brit. med. J.*] **1**, 1346–1349, May 13, 1961. 1 fig., 20 refs.

The world distribution of *Plasmodium falciparum* malaria (apart from changes brought about by recent eradication campaigns) parallels the distribution of an

inherited, sex-linked enzyme deficiency in the erythrocytes. Abnormally low glucose-6-phosphate dehydrogenase (G6PD) activity in the erythrocytes makes a patient susceptible to haemolysis when primaquine and certain other drugs are given. Deficient erythrocytes would be expected to provide a less suitable environment than normal erythrocytes for the metabolic requirements of the malaria parasite.

The authors suggest that this genetic abnormality, like the sickle-cell gene, may have survived in malarious areas because abnormal erythrocytes afford protection against lethal falciparum malarial infections. They examined 532 African children aged 4 months to 4 years in the Tanga and Korogwe districts of Tanganyika, where malaria transmission is high. Within this age group acquired immunity does not overshadow inherited resistance to malaria. The G6PD activity of the erythrocytes was determined by Motulsky's brilliant cresyl blue method (Motulsky, A. G., 1960, *Proceedings of Conference on Genetic Polymorphisms and Geographic Variations in Disease*, Ed. by B. S. Blumberg, Public Health Service, Washington, 1960) and the *P. falciparum* parasite rates and densities were estimated in thick blood films. Lower parasite rates and densities were present in enzyme-deficient than in normal children. The differences were statistically significant ($P<0.05$) in the males but did not quite attain significance in the females. Parasite rates were also low in subjects with the sickle-cell trait in the same population; the protection afforded by sickling was of the same order as that provided by G6PD deficiency in males, but was greater than that provided by enzyme deficiency in the females. Subjects with both genetic defects were not more strongly protected than those with only one.

An interpretation of the population genetics of G6PD deficiency is offered. The female heterozygote, being resistant to malaria, is at a selective advantage; the homo- or hemizygous male, being susceptible to haemolysis, may be at a net disadvantage and it is therefore possible for genetic equilibrium to be reached by natural selection. Haemolysis may perhaps be precipitated by virus infections. *L. G. Goodwin*

1400. **Chloroquine Resistance in *Plasmodium Falciparum***
M. D. Young and D. V. Moore. *American Journal of Tropical Medicine and Hygiene* [*Amer. J. trop. Med. Hyg.*] **10**, 317–320, May, 1961. 1 fig., 6 refs.

Resistance to chloroquine has recently been reported from several areas of South America. This paper from the National Institutes of Health, Bethesda, Maryland, describes studies on a strain of *Plasmodium falciparum* isolated in Colombia and transmitted by the inoculation of infected blood or by mosquitoes to 7 neurosyphilitic patients. Six of the patients failed to respond adequately or relapsed rapidly when chloroquine was given in a total dose of 2·1 g. Normally sensitive strains respond to 0·4 or 0·6 g. of chloroquine. In 2 instances 1·5 g. of chloroquine failed to control the parasitaemia; in 2 other patients the parasites continued to multiply in the blood after doses of 0·6 g. Drug resistance was still present after transmission by mosquitoes. The fact that the drug had been consumed by the patients was checked by determination of the plasma concentration, which was above 10 μg. per litre in each case, and by testing the urine for the excretion products of chloroquine.

The authors draw attention to the importance which widespread chloroquine resistance could have in malaria eradication campaigns. *L. G. Goodwin*

1401. **The Laboratory Diagnosis of Acute Hepatic Amoebiasis.** (Le diagnostic biologique de l'amibiase hépatique aiguë)
P. Beheyt, P. Charles, and S. Roberto. *Annales de la Société belge de médecine tropicale* [*Ann. Soc. belge Méd. trop.*] **41**, 93–126, April 30 [received Aug.], 1961. 38 refs.

The authors have studied at the Hôpital des Congolais, Leopoldville, amoebic liver disease as seen in 75 patients with liver abscesses, comparing these with another series of 104 patients with amoebic hepatitis without abscess formation.

The laboratory investigations carried out on each patient included blood cell counts, liver function tests, investigation of serum protein changes, determination of serum transaminase, serum cholinesterase, and serum mucoprotein levels, and of the erythrocyte sedimentation rate. In both series of patients the results of these laboratory tests were very similar. This finding, together with the success of specific anti-amoebic treatment with emetine or conessine, demonstrates the existence of an acute non-suppurative type of amoebic hepatitis. This was further confirmed by the subsequent development of abscesses in the liver in some patients in whom acute amoebic hepatitis had originally been diagnosed. *R. A. Neal*

1402. **The Treatment of Ankylostomiasis in Children with Bephenium Hydroxynaphthoate.** (Le traitement de l'ankylostomiase par l'hydroxynaphtoate de bephenium chez l'enfant)
R. Eloy. *Annales de la Société belge de médecine tropicale* [*Ann. Soc. belge Méd. trop.*] **41**, 29–33, Feb. 28 [received July], 1961. 5 refs.

At the Hospital of Luluabourg, Congo, 42 Congolese children, 8 of them less than 2 years old, were treated with bephenium hydroxynaphthoate (" alcopar "); all were heavily infected with hookworms and many were severely anaemic. Hookworm eggs were counted in coverslip preparations of fresh stools before treatment and one and 2 weeks afterwards. In 32 of the patients the egg count was reduced by 50 to 100% after a single dose of 5 g. of the drug (2·5 g. of the base) given with syrup to mask the bitter flavour. There were no side-effects of any kind and the author emphasizes the value of a safe anthelminthic such as alcopar which can be given even to quite young children within a few days of admission to hospital without any special preparation. The value of supplementary iron and other treatment was also increased and the stay in hospital shortened to 15 days for all but the severely protein-deficient patients. *L. G. Goodwin*

Allergy

1403. **Particle Size Produced by Various Instruments for Inhalation Therapy**
L. V. BERGMAN and J. E. SILSON. *Annals of Allergy* [*Ann. Allergy*] **19**, 735–748, July, 1961. 4 figs., 9 refs.

A plastic chamber has been evolved in which oiled slides are exposed to the sedimentation of aerosols produced by various types of nebulizer. The aerosol is blown into the box from an opening in its wall and, in the types of nebulizer tested, is generated either by compressing a rubber bulb or by means of a fluorohydrocarbon propellant. The slides are examined either by microphotography or visually, the latter method proving the more reliable. All of 4 commonly used types of nebulizer operated by hand pressure uniformly produced particles 80 to 90% of which had diameters below 3 μ and most of which were between 1·5 and 2·5 μ. The 2 nebulizers operated by a fluorohydrocarbon propellant produced slightly larger particles spread over a wider range. *H. Herxheimer*

1404. **Repository Treatment of Ragweed Pollinosis**
G. SOBEL. *Journal of Allergy* [*J. Allergy*] **32**, 288–301, July–Aug., 1961. 1 fig., 21 refs.

The author reports her results in 103 patients seen in private practice with ragweed pollen hay fever who were given one to three injections of a ragweed pollen emulsion in mineral oil. The relief of symptoms was satisfactory in 65% of the patients, as compared with 70% in a group of 70 patients who had received desensitizing treatment by means of multiple injections of an aqueous solution of pollen extract the previous year. Scratch tests with the emulsion gave positive reactions in 20% of all patients and 50% of those who had shown a general reaction after the injections. The reactions were mostly mild and occurred in 29% of the cases. In 2 cases a delayed local reaction occurred and in 4 patients pea-sized nodules at the site of the injections were present after 4 months. *H. Herxheimer*

1405. **Absorption Pattern of Ragweed Antigen and Active Sensitization in Man following Repository Pollen Injection**
M. GROLNICK, H. H. PELZ, and I-TSU CHAO. *Journal of Allergy* [*J. Allergy*] **32**, 327–332, July–Aug., 1961. 14 refs.

In a study of the immunological reaction following the injection of a repository preparation of ragweed pollen, carried out at the Jewish Hospital of Brooklyn, New York, by the reverse passive transfer technique, the undiluted serum of a patient strongly sensitive to ragweed was injected daily into the skin of allergic and non-allergic subjects after these had received an intramuscular injection of either a mineral emulsion of ragweed pollen or an ordinary aqueous extract of the pollen.

In subjects given the emulsion an erythematous indurated skin reaction appeared at the site of the serum injection 2 to 3 hours later, but in those given the aqueous solution this occurred after 30 to 45 minutes. In the former (emulsion) group this reaction persisted in non-allergic subjects for periods varying from 29 to 35 days and in one allergic subject for 15 days. In the group receiving the aqueous solution it persisted for 8 to 15 days in normal subjects and for 3 days in one allergic subject. Direct skin tests with ragweed extracts became positive in the normal subjects between 15 and 32 days after injection of the depot emulsion and remained so for up to 4½ months. These reactions could not be transferred passively. *H. Herxheimer*

1406. **Steroids in the Long-term Treatment of Asthma**
J. L. LIVINGSTONE and J. P. DAVIES. *Lancet* [*Lancet*] **1**, 1310–1314, June 17, 1961. 2 figs., 10 refs.

The authors record their experience at King's College and Brompton Hospitals, London, of long-term treatment with adrenal corticosteroids in 71 patients in whom this form of treatment was started between 1952 and 1958. All were severe asthmatics with mucopurulent sputum and the majority of them had been admitted to hospital for their first trial of steroids. The present series includes only those who responded initially to this treatment and of these approximately 90% have been followed up. The 30 male and 41 female patients studied ranged in age from 9 to 71 years, and the preceding history of asthma varied from 6 months to over 20 years; 19 of them had had attacks of status asthmaticus. Cortisone was the steroid used from 1951 to 1956, after which prednisone was preferred; however, 6 of the patients received triamcinolone or dexamethasone. The initial dose of prednisone was 40 mg. daily for 5 days, this being rapidly reduced to 15 mg. and then more slowly, when they became out-patients, to the lowest maintenance dose, which was usually between 7·5 and 12·5 mg. daily. Each patient was given a card stating the type and dose of the drug being administered as well as the names of the hospital and of the patient's own doctor.

Complications of treatment included the development of Cushingoid features, especially during treatment with cortisone, and weakness of leg muscles in one patient and marked hirsuties in another receiving triamcinolone. One woman with a known peptic ulcer had a haemorrhage while taking prednisone, and 2 patients developed spontaneous fractures of the ribs, accompanied in one case by collapse of a vertebral body. On the other hand one patient with cor pulmonale improved dramatically, the electrocardiogram returning to normal. The average period of treatment was 2¼ years. At the latest assessment the condition of 34 (48%) of the patients was classified as very good and of 26 (37%) as good, but in 11 (15%) the treatment failed. Patients with eosinophil granulocytes in the sputum before treatment responded

rather better than those with none. The authors conclude that prednisone is preferable to cortisone, but if possible the daily maintenance dose should not exceed 12·5 mg. No deaths were attributed to steroid treatment, nor were there any deaths from the asthma in this series. Deaths from asthma, however, occurred in 3 patients one of whom had stopped steroid treatment 12 months before, one whose maintenance dose of steroids was not increased when she went into status asthmaticus, and one who died in this condition without receiving steroid treatment.

[These findings confirm those of other workers that improvement in severe chronic asthma can be achieved and maintained by long-term treatment with adrenal corticosteroids.] *R. S. Bruce Pearson*

1407. **Delayed and Immediate Skin Reactivity in Man after the Injection of Antigen in Emulsion: Cell Transfer of the Delayed Sensitivity**
R. J. Becker, D. B. Sparks, S. M. Feinberg, R. Patterson, J. J. Pruzansky, and A. R. Feinberg. *Journal of Allergy* [*J. Allergy*] **31**, 229–235, May–June, 1961. 2 figs., 8 refs.

In an investigation carried out in the Department of Medicine, Northwestern University Medical School, Chicago, in which 15 non-allergic subjects received a depot injection of ragweed pollen in mineral-oil emulsion, 13 of them developed either immediate or delayed reactivity or both. All those who had the delayed type of reaction developed inflammatory swelling at the site of the injection. In 3 of these subjects the delayed sensitivity could be transferred to normal subjects by the injection of peripheral leucocytes. In contrast, when similar injections of ragweed-pollen emulsion were given to 27 ragweed-sensitive subjects no delayed reactions or local inflammatory swellings developed.

H. Herxheimer

1408. **Contact Sensitivity in Mice**
A. J. Crowle and C. M. Crowle. *Journal of Allergy* [*J. Allergy*] **32**, 302–320, July–Aug., 1961. 6 figs., 15 refs.

In experiments carried out at the University of Colorado School of Medicine, Denver, the authors have shown that if chlordinitrobenzene in acetone is brought in contact with the skin of a mouse, sensitivity develops within one week. On subsequent challenge skin testing there is an immediate reaction; this takes the form of a soft oedematous swelling which reaches its maximum in 3 hours and then recedes. After 6 hours a late reaction develops, this consisting in an indurated swelling which is maximum between 8 and 12 hours later and shows a central area of necrosis after 48 hours. The immediate type of reaction could be transferred to unsensitized mice by injection of the serum of the allergic animals, but the delayed type only by a suspension of thymus cells from the latter. A lysergic acid derivative (UML491) suppressed the immediate, but not the delayed, reaction, while cortisone suppressed only the latter. The antihistamine tripelennamine had no effect on either reaction. *H. Herxheimer*

1409. **Cyproheptadine in Treatment of Urticaria**
I. S. Bailey. *British Medical Journal* [*Brit. med. J.*] **2**, 430–431, Aug. 12, 1961. 6 refs.

Cyproheptadine ("periactin"), a new antihistamine and antiserotonin drug, was tried in the treatment of urticaria in 25 patients at Manchester Royal Infirmary, a double-blind technique being used. The patients received tablets containing either 2 mg. of cyproheptadine or lactose 3 times a day for 2 weeks, the results being assessed. In most instances patients were then given the alternative tablets for a further 2 weeks, at the end of which the results were compared. An excellent response was obtained in 15 patients receiving 6 mg. of cyproheptadine daily. Over a follow-up period of 6 months most patients remained well on a daily maintenance dose of 2 mg. Side-effects were minimal or unimportant.

G. B. West

1410. **On the Prophylactic Possibilities in ACTH Allergy.** [In English]
G. Rajka. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **16**, 159–167, 1961. 46 refs.

The literature on the incidence of allergic reactions to corticotrophin (ACTH) is reviewed and 3 illustrative cases are discussed in this paper from Karolinska Sjukhuset, Stockholm. Of the 3 patients, 2 had urticaria and one had a local reaction at the injection site and bronchial asthma. It was found that the responses to intracutaneous tests with ACTH and pituitary extracts of different sources were positive, whereas there was no reaction to animal tissues. A purified porcine preparation prepared by paper electrophoresis did not cause allergic reactions. In the author's view the findings provide supportive proof that inactive proteins and peptides are the cause of allergic reactions to ACTH. A decrease in ACTH allergy should occur with purer preparations. *A. W. Frankland*

1411. **Ten Cases of Occupational Hypersensitivity to Laboratory Animals.** [In English]
G. Rajka. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **16**, 168–176, 1961. 2 figs., 12 refs.

In this paper from Karolinska Sjukhuset, Stockholm, 10 cases of sensitivity to laboratory animals are described. All the patients were laboratory workers and 6 had a family history of an atopic disease. Most of the patients became sensitized in 3 to 6 months. The author emphasizes that all the patients had allergic rhinitis, while 4 also had asthma, 2 urticaria, and 2 Besnier's prurigo. In most of the cases the response to scratch tests was positive, but hair rather than an extract was the better antigen for this purpose. Some patients showed a group sensitivity to animals. In 3 patients there was sensitivity to pollen and hay and it is of interest that most of the animals lay on hay. Since in the circumstances contact with animals could not be avoided 5 patients received hyposensitization.

The author states that where contact is slight and the degree of sensitivity is low, tolerance may be expected to develop. *A. W. Frankland*

Nutrition and Metabolism

1412. **Plasma Cholesterol Levels in New Zealand: Observations in 1,000 Urban Males**
J. D. HUNTER and L. C. K. WONG. *British Medical Journal* [*Brit. med. J.*] **2**, 486–490, Aug. 19, 1961. 3 figs., 24 refs.

In a study carried out at the University of Otago, Dunedin, the fasting plasma cholesterol levels were determined in 500 manual workers and 500 "white-collar" workers, all apparently healthy, in an urban community. The mean values for the two groups were 224 and 238 mg. per 100 ml. respectively, the over-all mean being 231 mg. per 100 ml. At all ages the mean level was higher in the "white-collar" than in the manual workers, the difference being statistically significant in all 5-year age groups from 15 to 39. Taking the two groups together plasma cholesterol levels were lowest in the age group 15–19, rose steadily to a maximum in the age group 45–49, and then slowly declined. Only in the age group 20–39 were the levels significantly higher in grossly overweight subjects than in the others. Division of the 450 subjects in the most important age group, namely, 40 to 59, into non-smokers and light, moderate, and heavy smokers revealed that the plasma cholesterol levels did not differ with different smoking habits.

M. Lubran

METABOLIC DISORDERS

1413. **Phenylketonuria Treated with a High Phenylalanine Intake and Casein-hydrolysate/Aminoacid Mixtures**
S. O'DALY. *Lancet* [*Lancet*] **1**, 1379–1383, June 24, 1961. 4 figs.

In this preliminary communication from the National Children's Hospital, Dublin, the case is first described of a 6-year-old boy suffering from phenylketonuria in whom the serum phenylalanine level became normal when he was treated with an amino-acid–casein hydrolysate mixture containing 40 g. of casein (nitrogen 11·5%), 2·5 g. of L-tyrosine, 0·8 g. of DL-tryptophan, and 0·5 g. of DL-methionine, with carbohydrate, fat, and minerals to 100 g. This normal level was maintained even when the additional protein intake was raised to 1·5 g. per kg. body weight per day, but when it reached 2·3 g. per kg. per day (phenylalanine 120 mg. per kg.) the serum phenylalanine level rose above 10 mg. per 100 ml. and phenylalanine and its abnormal metabolites reappeared in the urine. It was originally thought that the product had a specific effect independent of its low phenylalanine concentration. This boy was then further studied together with 2 mentally defective women aged 19 and 26 years respectively with mild ketonuria in order to ascertain the effect of the hydrolysate on the phenylketonuria. Examination of the urine of all 3 patients by qualitative chromatography and the ferric chloride test showed that there was a decreased excretion of phenylpyruvic acid, *o*-hydroxyphenylacetic acid, and phenylalanine which coincided with the decreased serum levels. (It was not possible to perform nitrogen balance studies.) Administration of the casein hydrolysate–amino-acid mixture, with an adequate but not high protein intake, was accompanied by a small but significant decrease in the serum phenylalanine level.

As these observations were in some respects contradictory, the author suggests that phenylalanine, by its high concentration in the serum and the presence of its abnormal metabolites, creates such a disturbance in the metabolic pathways of other amino-acids as to cause them to be relatively deficient and so indirectly to inhibit its own incorporation into protein. Thus below a critical level of protein intake these mutual inhibitions would result in a general protein depletion; but above such a level it is possible that they would lead primarily to a selective depletion only of those proteins with a high content of both phenylalanine and any one or more of the other amino-acids involved in the disturbance. Therefore, in suggesting a deficiency of phenylalanine in the protein pool it is not necessary to postulate the formation of abnormal proteins; nor is this suggestion in conflict with the finding of Block *et al.* (*J. biol. Chem.*, 1940, **134**, 567) that there was no significant difference between the phenylalanine content of several organs, including the brain, of a phenylketonuric patient and a normal control subject. Further experiments, including nitrogen and phenylalanine balance studies and comparison of the efficiency of utilization of dietary nitrogen in phenylketonurics and controls, are planned.

S. M. Hardy

1414. **Effect of D-Thyroxine on Serum Cholesterol**
R. GREENE, J. F. PEARCE, and D. F. RIDEOUT. *British Medical Journal* [*Brit. med. J.*] **1**, 1572–1575, June 3, 1961. 23 refs.

It has been shown by Greene and Farran (*Brit. med. J.*, 1958, **2**, 1057; *Abstr. Wld Med.*, 1959, **25**, 271) and confirmed by other workers that D-thyroxine is the only analogue of thyroxine that is capable of reducing the serum cholesterol level without entailing the risk of precipitating ischaemic heart disease. At the Royal Northern and New End Hospitals, London, 24 patients with hypercholesterolaemia were treated with this drug in doses ranging from 5 to 15 mg. daily for periods varying from 8 to 26 weeks. In 18 of these patients a satisfactory reduction in the serum cholesterol level was produced. The most satisfactory results were obtained in patients with diabetes and atherosclerosis, 15 of the 19 patients with these disorders showing a satisfactory response, while 3 of the 4 patients with idiopathic hypercholesterolaemia also responded favourably, though in regard to this latter group no conclusions could be drawn because of the small numbers. The single patient with disseminated lupus erythematosus did not respond. The

authors point out, however, that how far the lowering of the serum cholesterol level to normal is of benefit to the patient is still an open question which remains to be answered. *R. Schneider*

1415. **Management of Familial Hemochromatosis**
W. G. Frey III, J. Milne, G. B. Johnson Jr., and F. G. Ebaugh Jr. *New England Journal of Medicine* [*New Engl. J. Med.*] **265**, 7–12, July 6, 1961. 8 figs., 28 refs.

From the Veterans Administration Hospital, White River Junction, Vermont, the cases of 6 men with haemochromatosis are briefly described to illustrate the familial incidence of the disease and to stress the importance of liver biopsy in diagnosis and in the control of treatment.

The first patient was 50 when the diagnosis of haemochromatosis was made by liver biopsy. Venesection was started 7 years later, and continued for 3 years: iron disappeared from the bone marrow and there was a slight anaemia, but the cirrhotic liver still contained excess iron. Further venesection in the next 3 years, to a total of 84 litres, brought clinical improvement. In the second patient the condition was diagnosed by liver biopsy at the age of 42; though 18 litres of blood were removed between the ages of 47 and 52 he continued to deteriorate. In the next 18 months 53 litres were removed, whereupon iron disappeared from the bone marrow, its amount decreased in the liver, and the patient improved clinically. His father, the third patient, died at the age of 71 with haemochromatosis and hepatoma. The fourth patient, a son of Patient 2 and grandson of Patient 3, was well at the age of 27, with a normal serum iron level and no excess iron in the bone marrow. But liver biopsy showed the presence of excess iron and still did so after the removal of 9·5 litres of blood in 6 months, which induced hypochromic anaemia and lowered the serum iron level. The fifth patient, aged 64, was found to have a large liver: biopsy showed excess iron in it, but not in the skin or bone marrow. His brother, the sixth patient, died at the age of 62 with haemochromatosis and hepatoma, both diagnosed by liver biopsy.

The authors suggest that the disease occurs in families more often than has been thought, is best diagnosed by liver biopsy, and needs energetic treatment.
G. C. R. Morris

1416. **Excretion of Porphobilinogen and δ-Aminolaevulinic Acid in Acute Porphyria**
B. Ackner, J. E. Cooper, C. H. Gray, M. Kelly, and D. C. Nicholson. *Lancet* [*Lancet*] **1**, 1256–1259, June 10, 1961. 1 fig., 17 refs.

Twelve patients known to have suffered from acute porphyria were studied at the Maudsley Hospital, London. In addition, 2 patients in the early recovery stages of an acute attack were studied at other London hospitals and one of these studied again on readmission for an acute attack. The urinary excretion of porphobilinogen and δ-aminolaevulinic acid was measured and compared with the clinical findings. Although there was a very rough correlation between the excretion of these compounds and the severity of the clinical condition, some patients excreting considerable quantities of these compounds were symptomless. Furthermore, fluctuations in excretion in particular individuals were not correlated with changes in symptomatology. It is concluded that the excretion of these metabolites and the changes in the nervous system are separate manifestations of a metabolic event or series of events.
H. Harris

1417. **The Therapeutic Effect of Adenosine-5-monophosphoric Acid in Porphyria**
A. Gajdos and M. Gajdos-Török. *Lancet* [*Lancet*], **2**, 175–177, July 22, 1961. 3 figs., 9 refs.

A satisfactory treatment for porphyria has yet to be discovered, largely because the mechanism behind the various clinical symptoms which appear in porphyria remains unknown despite much clinical and biochemical study. Since the porphyrins and their precursors are themselves practically non-toxic, one possible mechanism could be that the increased synthesis of these substances leads to a deficiency of other essential metabolites. On the basis of recent experimental observations by various workers, which are briefly recapitulated, it is postulated that a deficiency of phosphorylated derivatives of adenosine during porphyria might be responsible for the clinical signs. With this in mind the authors and colleagues, working at the Hôtel-Dieu, Paris, tentatively treated one patient suffering from severe porphyria with a series of intramuscular injections of adenosine-5-monophosphoric acid (A.M.P.) in a dose of 250 mg. daily; the results were very encouraging, for within 5 days the symptoms and the urinary excretion of uroporphyrin disappeared completely. Subsequently, 9 other patients with porphyria were treated with A.M.P., with good therapeutic effect in 7 of them as judged by the clinical and biochemical signs. The possibility of spontaneous remission, however, makes it difficult to assess accurately the efficacy of the treatment.

The effect of A.M.P. on experimental porphyria in animals was therefore investigated. In view of the report of Cam (*Bull. Soc. méd. Hôp. Paris*, 1960, **76**, 1305) that several thousand cases of human porphyria recently occurred in Turkey in subjects who had consumed wheat containing 0·1 to 0·2% of hexachlorobenzene, a similar form of porphyria was induced in rats by mixing hexachlorobenzene with the diet in a proportion of 2%. The oral administration of 20 mg. of A.M.P. daily had a highly beneficial effect on the clinical symptoms and in limiting the extent of liver damage and reduced the excessive formation of porphyrins and porphyrin precursors. In further experiments porphyria was induced in chick and duck embryos by injecting allyl*iso*propylacetamide (A.I.A.) into the yolk sac; injection of A.M.P. simultaneously was followed by better results than were found in the control group. On the other hand when porphyria was induced in rabbits by adding A.I.A. or allyl*iso*propylcarbamide to the diet the oral administration of A.M.P. had no beneficial effect. As the authors point out, there is not yet sufficient proof that their working hypothesis is correct, but they do consider that these early results warrant further investigation. *Joseph Parness*

Gastroenterology

STOMACH

1418. **Some Metabolic and Haematological Effects of Oesophago-jejunostomy with By-pass of the Stomach**
S. T. CALLENDER, L. J. WITTS, P. R. ALLISON, and A. GUNNING. *Gut* [*Gut*] **2**, 150–157, June, 1961. 3 figs., 12 refs.

A study of 12 patients on whom oesophago-jejunostomy had been performed leaving the stomach *in situ*, together with careful investigation of the resulting metabolic changes, is reported from the Radcliffe Infirmary, Oxford.

Serum cyanocobalamin levels as well as absorption of labelled cyanocobalamin were estimated, and iron absorption was studied by means of an oral dose of ferrous sulphate containing 5 mg. ^{59}Fe. Absorption of fat and of D-xylose was also studied.

Cyanocobalamin deficiency was a constant finding, and the serum level of cyanocobalamin was below 100 $\mu\mu$g. per ml. in all patients except 3 who were receiving injections of cyanocobalamin and one who was taking oral tablets of the vitamin. The absorption of radioactive cyanocobalamin was reduced in all cases, with values " in the range for pernicious anaemia, although the mean absorption for the group (22%) was somewhat greater than the mean for pernicious anaemia ". Though steatorrhoea was present, often in considerable degree, administration of intrinsic factor was effective in enhancing the absorption of cyanocobalamin. Xylose was absorbed normally. Examination of jejunal biopsy specimens usually yielded normal results.

The reason for the development of cyanocobalamin deficiency after oesophago-jejunostomy by-passing the stomach is not clear. Iron absorption was impaired, but not to the degree found in steatorrhoea. The procedure has now been abandoned in favour of oesophago-jejuno-gastrostomy, and the authors are hopeful that this new technique will avoid the severe metabolic effects they describe. *I. McLean Baird*

1419. **ABO Blood Groups of Siblings of Gastric Ulcer and Gastric Carcinoma Patients**
J. A. BUCKWALTER and R. E. VAN SCOY. *British Medical Journal* [*Brit. med. J.*] **1**, 1585–1587, June 3, 1961. 6 refs.

In an investigation carried out at the University of Iowa and Iowa City Veterans Administration Hospitals, the authors found increased frequency of Group-O blood in patients with gastric ulcer and in their siblings compared with controls. In patients with gastric carcinoma and their siblings there was an increased frequency of Group-A blood compared with controls, but here the differences were not statistically significant.
A. Gordon Beckett

LIVER

1420. **Cirrhosis of the Liver and Decreased Arterial Oxygen Saturation**
W. H. ABELMANN, G. E. KRAMER, J. M. VERSTRAETEN, M. A. GRAVALLESE JR., and W. F. MCNEELY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **108**, 34–40, July, 1961. 22 refs.

Some patients with hepatic cirrhosis are known to develop unsaturation of the arterial blood with oxygen. In this report from the Boston City Hospital and Harvard Medical School the mechanism underlying this finding has been investigated in 34 cirrhotic patients, in all but one of whom the cirrhosis was associated with alcoholism; none of these patients had coexistent lung or heart disease. Patients with tense ascites were also excluded because of the possible effects of this factor on pulmonary function.

It was found that the mean arterial oxygen saturation in the cirrhotic group was 93·2% (S.D.$\pm$2·5) compared with 95·8% (S.D.$\pm$1·4) in 20 normal subjects, the difference being significant ($P<0{\cdot}01$). There was also a significant lowering of the arterial oxygen tension in the cirrhotic group. Alveolar–arterial pressure gradients were elevated (mean 26 mm. Hg) in 5 cirrhotics breathing room air as compared with normal subjects (mean 10 mm. Hg) under the same conditions. This level fell to normal on breathing low oxygen mixtures, suggesting (in the presence of a diffusing capacity for oxygen which was normal) venous admixture. The latter factor was found to be increased to the extent of 8 to 20% of the cardiac output in the cirrhotic patients.

The authors discuss the possible sites of the vascular anastomoses responsible for producing arterial unsaturation, mentioning the opening up of pulmonary arteriovenous fistulae and, as a more likely site, the development of communications between the portal and pulmonary venous systems. Whatever the site of the abnormality, it may be that the development of arterial desaturation predisposes to further hepatic cellular injury and at the best cannot be of any advantage to a cirrhotic patient. *A. E. Read*

1421. **Formiminoglutamic Acid (FIGLU) Excretion in Hepatic Cirrhosis**
F. C. CARTER, P. HELLER, G. SCHAFFNER, and R. J. KORN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **108**, 41–46, July, 1961. 1 fig., 26 refs.

In patients with folic acid deficiency increased excretion of formiminoglutamic acid (FIGLU) in the urine can be demonstrated. This substance is an intermediate metabolite in the degradation of histidine. A histidine loading test can be used to increase the FIGLU excretion so that it can be detected in the urine. At the Veterans Administration West Side Hospital and University of

Illinois, Chicago, the excretion of FIGLU has been studied in 30 patients with alcoholic cirrhosis, a condition in which a megaloblastic anaemia responding to folic acid sometimes develops, and in 8 control subjects without hepatic disease, malnutrition, or anaemia. A 5-day test was evolved, 24-hour urine collections being performed and 5 g. of histidine 3 times a day being given alone on the 2nd day and accompanied by 20 mg. of folic acid 3 times a day on the 4th and 5th days. The total excretion of FIGLU on the 2nd and 3rd days was measured and expressed as the "maximal FIGLU excretion". The amount excreted on the 4th or 5th day, whichever was the lower, was deducted from the initial 48-hour value and this difference, expressed as a percentage of the "maximal FIGLU excretion", was called the "maximal correction".

In the control subjects the urinary excretion of FIGLU after histidine loading was 0 to 38 μM in 48 hours and in the 30 cirrhotic patients 3 to 18,100 μM. The 2 highest values in the cirrhotic group were in patients with frank megaloblastic blood changes. In 29 of 30 cirrhotic patients the FIGLU excretion was increased. The percentage correction with folic acid ranged from 15 to 100%. Sixteen of 22 patients studied in this way showed corrections of 50 to 100% and only 5 showed full correction. There appeared to be no correlation between the level of excretion of FIGLU and the patient's clinical condition, but there did seem to be a more marked excretion in patients in whom liver biopsy showed severe necrosis.

In discussing these abnormalities the authors point out that folic acid deficiency as determined by this technique thus appears to be a common finding in alcoholic cirrhosis. The cause of such a deficiency may be variable—poor diet, malabsorption, and deranged liver function being possible factors in its production.

A. E. Read

1422. **A Study of the Effects of Albumin Infusions in Patients with Cirrhosis of the Liver**

P. W. Dykes. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **30**, 297–327, July, 1961. 4 figs., bibliography.

The author has studied, at the Queen Elizabeth Hospital, Birmingham, the effect of intravenous infusions of albumin in 13 patients with advanced hepatic cirrhosis, all of whom had persistent ascites and oedema resistant to orthodox measures. The amount of albumin infused varied from 100 to 1,800 (mean 1,120) g., usually administered in lots of 25 g.; in the successful cases total amounts up to 4,750 g. were given in maintenance courses. The results were good in 7 patients, with complete elimination of oedema and ascites for periods up to 3 years. Of 10 patients receiving the full course of treatment, 8 greatly improved generally. Complications included fatal febrile reactions in 2 cases, temporary jaundice in 2, severe unexplained proteinuria in one, and severe gastro-intestinal haemorrhage in 3 patients. Several patients survived for much longer periods than could have originally been expected.

In 10 patients the serum albumin level rose steadily to 4 g. per 100 ml. within 22 days, while the ascitic fluid albumin content rose less. The plasma globulin concentration fell, but the ascitic content rose; the albumin: globulin ratio in the ascitic fluid remained constant at 13% above that in the plasma. From three to four times the amount of albumin, as calculated from studies with ^{131}I-labelled albumin, was actually needed to raise serum albumin concentrations to normal. This was thought to be due in part to increased catabolism, but mainly to movement into depleted cells. Successful diuresis was considered to be due to the expansion of blood volume, and elimination of the ascites to increasing colloid osmotic pressure, which was studied in detail. A serum albumin concentration of less than 130 mEq. per litre and a protein concentration of 1 g. per 100 ml. in ascitic fluid were noted in patients who did not respond to therapy.

[A thoughtful and detailed paper.] *Arnold Pines*

1423. **Further Evaluation of Splenic Pulp Manometry as a Differential Diagnostic Test of Acute Upper Gastro-intestinal Bleeding**

L. M. Rousselot, W. F. Panke, and A. H. Moreno. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **35**, 474–487, May, 1961. 4 figs., 9 refs.

In this paper the authors present a further report on emergency splenic pulp manometry as a method of establishing the presence of oesophageal varices in cases of upper gastro-intestinal bleeding. The previous investigation (*Surg. Gynec. Obstet.*, 1959, **109**, 270; *Abstr. Wld Med.*, 1960, **27**, 283) had indicated that the method provided a 90% accuracy in determining the existence or otherwise of varices, and the present study has confirmed the impression.

In 165 cases admitted to St. Vincent's Hospital, New York, with active or recent haemorrhage splenic pulp manometry and portography were carried out either during an acute haemorrhage or after bleeding had ceased. Of the 116 patients examined after bleeding had ceased, 71 were shown to have oesophagogastric varices and the remaining 45 to have bled from other lesions. In the remaining 49 patients manometry was performed as an initial differential diagnostic test during an acute haemorrhage, and in 24 of these patients varices were established as the cause.

The splenic pulp pressure of patients bleeding from varices was always higher than that of patients losing blood elsewhere, irrespective of the relationship of manometry to the acute episode. In patients bleeding from varices the mean pressures taken under emergency conditions and subsequent to the haemorrhage were respectively 424·4 mm. and 406·5 mm. of water. The corresponding pressures in patients bleeding from other sites in the upper gastro-intestinal tract were 176·4 mm. and 178 mm. of water. All patients with a splenic pulp pressure greater than 290 mm. of water had bled or were still bleeding from oesophageal varices, and with one exception all patients with a pressure below 250 mm. of water had had a haemorrhage or were still bleeding from a lesion other than varices. Thus there was only a very narrow range of equivocal pressures, and only 15 of the readings (4 of them emergency ones) fell into this zone. Of the patients who bled from varices, 93% had a pressure

greater than 290 mm. of water and 54% of them had readings greater than 400 mm.

The procedure has not been followed by any complications or significant morbidity in the present series, although emergency splenic puncture could not be completed in 3 cases.

In the opinion of the authors this is a relatively simple procedure that does not require complex apparatus and may therefore be used in hospital as a routine diagnostic procedure irrespective of the availability of laboratory or x-ray technicians. It is of special value in patients with clinical evidence of hepatic cirrhosis who are losing blood from sites other than oesophageal varices.

J. Warwick Buckler

INTESTINES

1424. **Assessment of Intestinal Activity with the Aid of Enzymatic Indices in Diseases of the Alimentary Tract.** (Оценка деятельности кишечника при помощи ферментных показателей при заболеваниях пищеварительного тракта)

S. Ja. Mihlin. *Клиническая Медицина* [*Klin. Med. (Mosk.)*] **39**, 61–67, July, 1961. 21 refs.

Enzymatic indices may facilitate the detection of obscure disorders of the intestine and may help in the differentiation of intestinal affections, such as dysentery, sprue, and food poisoning. They may also be of use in the assessment of the condition of the intestine during the course of the disease and upon clinical recovery.

A. Orley

1425. **The Measurement of Gastrointestinal Protein Loss by a New Method**

K. N. Jeejeebhoy and N. F. Coghill. *Gut* [*Gut*] **2**, 123–130, June, 1961. 4 figs., 8 refs.

This paper from the West Middlesex Hospital, Isleworth, describes a new method of estimating protein loss from the alimentary tract in which radio-iodinated human serum albumin (R.I.H.S.A.) is used. Hitherto radio-iodinated polyvinyl pyrrolidine (^{131}I-PVP) has been employed for this purpose, but this new method has been found to overcome many of the disadvantages of the ^{131}I-PVP technique and to be able to detect abnormal protein loss not detected with the synthetic polymer. Methods for the determination of protein turnover and the quantitative estimation of protein excretion in the intestine are described in detail. The use of "amberlite" resin IRA-400 in absorbing the products of digestion of excreted R.I.H.S.A. is described and its efficiency assessed at about 80%. In addition, the faecal radioactivity after intravenous injection of ^{131}I-PVP was studied.

The half-life and daily turnover of R.I.H.S.A. were determined in 19 patients, who were divided into four groups: (1) a control group of 3 patients without intestinal disorder; (2) 4 patients with inactive gastro-intestinal disorders; (3) 8 patients with gastro-intestinal disease but without hypoproteinaemia or oedema; and (4) 4 patients who in addition had hypoproteinaemia and oedema. The albumin turnover studies indicated that there was no relation between the half-life of R.I.H.S.A. and the presence of hypoproteinaemia and oedema in patients with disease of the small intestine. Possible explanations for this are discussed. A study of faecal radioactivity, using R.I.H.S.A., indicated that albumin is lost from the metabolic pool in two ways—one-half by endogenous breakdown and one-half by gastro-intestinal loss. In the groups studied it was shown that patients without hypoproteinaemia or oedema had greater endogenous breakdown than intestinal loss. In the last group of patients, however, who had hypoproteinaemia and oedema there was a marked increase in excretion of R.I.H.S.A., which was not detected by ^{131}I-PVP. By means of these methods it was possible to demonstrate a significant decrease in R.I.H.S.A. excretion following the treatment of patients with coeliac disease with a gluten-free diet, and the authors suggest that the methods described may be fruitful in the study of treatment of other diseases of the small intestine.

J. S. Malpas

1426. **Proctalgia Fugax**

H. Ibrahim. *Gut* [*Gut*] **2**, 137–140, June, 1961. 19 refs.

The author, at Kasr-el-Aini University Hospital, Cairo, has studied 24 patients aged between 18 and 65 years suffering from proctalgia fugax. This term was first used by Thaysen in 1935 (*Lancet*, 1936, **2**, 793), although proctalgia was described by Myrtle in 1883 (Ewing, *Brit. med. J.*, 1953, **1**, 1083). The condition, which occurs infrequently, more commonly affects males than females, occurs between the ages of 20 and 50, though it sometimes begins in early childhood, and shows a familial tendency. It is rare among the poorer Egyptian working classes, but accounts for 4% of all cases of rectal disease among Cairo University students.

Of the 24 patients studied, 15 were men (average age at onset 21 years) and 9 women (average age at onset 31 years). In the men the attacks gradually increased in severity to reach a peak at about 26 to 30 years of age, thereafter becoming milder and more infrequent. In the women the phase of severity was more prolonged, sometimes continuing to the age of 50. The onset was marked by nocturnal attacks of pain in the rectum, the severity of which increased with succeeding attacks; the pain was accompanied by abdominal cramps, nausea, sweating, and syncope. Attacks might last 10 to 15 minutes and occurred every 3 or 4 weeks. The author classifies the attacks into "grand mal" and "petit mal", according to whether or not they are accompanied by syncope. In "grand-mal" attacks he describes an "aura" localized to the lower abdomen; severe pain is felt high in the rectum and the patient loses consciousness. Among the exciting causes are coitus and colitis.

On the basis of Bolen's (*New Engl. J. Med.*, 1943, **228**, 564) sigmoidoscopic findings of swollen mucosa, prominent vessels, and obstruction at the rectosigmoid junction the author postulates a sudden vascular congestion analogous to migraine as the precipitating factor. His treatment consists in reassurance, avoidance of known precipitating causes, and adoption of a right lateral position with pressure on the anus. [No reference is made to the use of antimigrainous drugs.]

J. S. Malpas

Cardiovascular System

1427. **Clinical and Haemodynamic Patterns in Endomyocardial Fibrosis**
J. P. SHILLINGFORD and K. SOMERS. *British Heart Journal* [*Brit. Heart J.*] **23**, 433–446, July, 1961. 15 figs., 14 refs.

Endomyocardial fibrosis, a disease endemic in certain parts of Africa, involves predominantly the endocardium and myocardium of the ventricles, especially in the region of the atrioventricular ring, where it gives rise to mitral and tricuspid incompetence. Fifteen patients (presenting with symptoms of heart failure) in whom the diagnosis was made on clinical grounds, were studied at Mulago Hospital (Makerere College), Kampala, Uganda. Mitral incompetence was found in 12 cases and a right ventricular heave or a loud pulmonary second sound suggesting pulmonary hypertension also in 12. In 4 of these and in one other tricuspid incompetence was present. A left ventricular third heart sound was an invariable sign and in 9 patients a right ventricular third sound was heard at the lower end of the sternum.

On cardiac catheterization the X and Y descents in the right atrial pressure tracing were often relatively increased, suggesting constriction of the ventricle, but in 4 patients with tricuspid incompetence the X descent was impaired. The right ventricular tracing almost invariably showed a raised end-diastolic pressure and an early diastolic dip, but with more severe disease distorted tracings resembling those found in the right atrium were obtained, suggesting that the function of the right heart had been taken over by the atrium. Moderate pulmonary hypertension (systolic pressures of 45 to 60 mm. Hg) was found in 10 patients, and in one a pressure of 90 mm. Hg. The pulmonary capillary pressure pulse in most patients with pulmonary hypertension reflected a raised left atrial pressure, but it gave no guide in distinguishing constriction of the left ventricle from left ventricular failure due to other causes.

Right heart catheterization, while confirming the clinical findings, was considered to be of little value in differential diagnosis, although a grossly abnormal right ventricular pulse was suggestive evidence of endomyocardial fibrosis. *Eirian Williams*

1428. **Changes in Blood after Using an Extracorporeal Circulation**
A. L. BLOOM. *British Medical Journal* [*Brit. med. J.*] **2**, 16–20, July 1, 1961. 1 fig., 33 refs.

In this communication from the General Infirmary at Leeds the author describes the haematological changes occurring during the use of extracorporeal circulation, the study being based on 13 cases selected at random from a series of patients undergoing open heart surgery for which the Melrose oxygenator was used without hypothermia. Blood samples were taken before, during, and after perfusion and polymorphonuclear, lymphocyte, eosinophil, and platelet counts carried out. In addition, thrombin times and one- and two-stage prothrombin times were determined, thromboplastin generation tests and antihaemophilic globulin assays performed, and plasma fibrinogen and euglobulin lysis times estimated.

It was found that a marked fall in the platelet count occurred after perfusion in 12 of the 13 cases, though purpura was not seen in any of them. A neutrophil leucocytosis occurred during perfusion, whereas a decrease in the number of lymphocytes and of neutrophil and eosinophil granulocytes was noted at the end of the operation. A fall was noted in the plasma fibrinogen level in 10 of the 13 cases, though one case showed a rise. There was postoperative evidence of increased fibrinolysis, after an initial fall, in 9 out of 13 cases immediately after perfusion, this change being marked and therefore of more significance in 5; however, no patient in this series developed a haemorrhagic tendency due to fibrinogenopenia and excess fibrinolysis. Coagulation studies were complicated by the necessary use of heparin. An attempt to overcome this was made by determining thrombin times with and without the addition of toluidine blue. The presence of heparin prolongs the clotting time, while the addition of toluidine blue to plasma corrects the thrombin time and confirms the presence of heparin. Blood taken after the use of the extracorporeal circulation showed unneutralized heparin to be present in 6 out of the 7 cases investigated, in spite of the administration of protamine sulphate. In nearly all cases there was no significant change in results of the one- and two-stage prothrombin tests. Two cases showed diminished antihaemophilic globulin levels, while 3 showed an unexpected rise. The serum thromboplastin generation tests for Christmas factor revealed no significant alteration.

The literature is surveyed and possible causes for the results in the present series considered. Apart from the obvious trauma and exposure to contact with numerous foreign surfaces, the fall in the platelet count may be due to the use of heparin or protamine. The role of ACTH produced in response to stress is considered as a possible cause of the leucocyte changes, but an increased rate of removal of damaged cells may also have been responsible. The author points out the hitherto unrecognized phenomenon of early decreased fibrinolysis and discusses the various changes observed in coagulation factors. The presence of unneutralized heparin is a potent source of troublesome bleeding and can be obviated by the use of hexadimethrine bromide to neutralize its activity. *J. S. Malpas*

1429. **Studies on Electrocardiographic Changes during Exercise Tests.** [Monograph, in English]
L. SANDBERG. *Acta medica Scandinavica* [*Acta med. scand.*] **169**, Suppl. 365, 1–117, 1961. 50 figs., bibliography.

1430. **The Infrequent Normal Electrocardiogram in Cardiac Pain**
W. Evans and H. G. Lloyd-Thomas. *American Heart Journal* [*Amer. Heart J.*] **62**, 51–64, July, 1961. 23 refs.

This is an analysis from the London Hospital of some 7,000 electrocardiograms (ECGs) recorded over a period of 15 years from 3,546 patients complaining of chest pain and subsequently followed up. The ECG leads used were I, II, III, and IIIR (Lead III in inspiration) and the chest leads CR_1 (sometimes CR_2), CR_4, and CR_7. Unipolar limb leads were found "manifestly inferior to CR leads in the portrayal of the significant lesser electrocardiographic changes".

About half of the 2,500 patients presenting with pain of cardiac origin had changes of frank myocardial infarction, another half showed the lesser changes of limited cardiac infarction, which are described in detail, while a small group of 46 patients with cardiac pain resulting from temporary ischaemia had a changing ECG tracing, abnormal at one time, normal at another time. In the remaining cases, in which the chest pain was in every way typical of cardiac pain, the resting ECG was normal and remained normal, while an exercise ECG never showed evidence of coronary insufficiency.

The authors believe that a strictly normal ECG excludes cardiac pain if recorded during a period when the patient is liable to paroxysms of pain, even should the description of his symptoms indicate a coronary arterial source. It is suggested that the exercise ECG can play a part in assessing the significance of lesser ECG signs found during a routine medical examination when no history of pain is elicited. *T. Semple*

1431. **The Vectorcardiogram before and after Myocardial Infarction. Superimposition of Serial Loops**
L. Wolff, M. D. Samartzis, and R. Wolff. *American Heart Journal* [*Amer. Heart J.*] **62**, 22–30, July, 1961. 6 figs., 5 refs.

This is a study from the Beth Israel Hospital and Harvard Medical School, Boston, of serial, superimposed vectorcardiographic (VCG) tracings from 10 patients before and after a first myocardial infarction and from 9 patients before and after a second infarction. The VCG loops were transferred to white cards by projection through a photographic enlarger and thus accurate superimposition was obtained. In each case 3 pairs (horizontal, sagittal, and frontal) of superimposed "before" and "after" loops as well as electrocardiograms and orthogonal Leads X, Y, and Z were obtained. Necropsy was performed on 4 of the 19 patients and in all of these the VCG diagnosis was confirmed.

The technique demonstrated diagnostic changes very clearly, notably the earliest superiorly orientated forces in inferior myocardial infarction and the increased magnitude of the posterior vector located within 0·045 second after the onset of the QRS loop in anterior infarction.

VCG signs of infarction in multiple cases may occur in association with a single acute episode. Pre-existing signs of infarction may lessen after a second infarction, but when the second infarct is in the same location as the first the diagnostic signs increase. *T. Semple*

CONGENITAL HEART DISEASE

1432. **The Clinical Picture and Diagnosis of Isolated Pulmonary Stenosis.** (Клиника и диагностика изолированного стеноза легочной артерии у детей)
N. G. Zernov. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **6**, 26–30, June, 1961. 3 refs.

Isolated pulmonary stenosis is an acyanotic form of congenital heart defect occurring in the absence of right heart failure; the latter is usually the terminal event and is liable to develop before the end of the third decade. The stenosis may, however, be compatible with fair health for some years, and in 11 out of the 52 cases (occurring in 30 girls and 22 boys aged 6 to 16) reviewed here it was found in the course of examination for other diseases. The main symptoms are fatiguability, dyspnoea on exertion, tachycardia, and disagreeable sensations or pain in the precordium in a young person. Clinical examination reveals tachycardia, dilatation of the jugular veins, extension of the area of cardiac dullness to the right, and a systolic murmur and thrill over the 2nd (sometimes the 3rd) left intercostal space. The arterial blood pressure is low and the venous pressure high.

Electrocardiography shows marked right predominance, with deep waves at S2 and S3 and absent or negative T3. Radiographs of the chest reveal pale lung fields, a large right ventricle and auricle, and often dilatation of the pulmonary arch. Angiocardiography confirms the delay in emptying of the right ventricle and pulmonary arteries, while in some cases the actual stenosis can be demonstrated. On cardiac catheterization the pressure is found to be much raised in the left ventricle (as high as 168 mm. Hg in some cases), but is very low in the pulmonary artery (15 to 34 mm. Hg); this steep gradient is pathognomonic. In view of the grave prognosis—and in spite of the mild early symptoms—operation is the only treatment likely to help children with this defect. Of the author's 52 cases, 46 were successfully so treated. He considers 5 to 8 years to be the optimum age for operation. *L. Firman-Edwards*

1433. **The Surgical Treatment of Pulmonary Stenosis**
R. Brock. *British Heart Journal* [*Brit. Heart J.*] **23**, 337–356, July, 1961. 3 figs., 23 refs.

In this article, which is based on the 1960 St. Cyres Lecture, the author reviews his unique experience of the treatment of pulmonary valvular stenosis in nearly 200 patients. It is estimated that the incidence of this condition is between 10 and 14% in all cases of congenital heart disease and may be associated with a variety of additional malformations. It is probable that the majority of patients with valvular stenosis of any severity do not live much beyond adult life, though a number of exceptions have been recorded. The author re-emphasizes that the indications for operation must be based on the necessity for relieving obstruction and avoiding right ventricular strain. The original figure that surgeons accepted as being an indication for operation was a right ventricular pressure of 60 to 70 mm. Hg, but this record

is obtained during resting conditions and may almost double during exercise. There can be little doubt that when a high range of ventricular pressures are found there is an absolute indication for the relief of the obstruction.

Of the 198 patients treated, 74 were cyanotic and 124 acyanotic, but the recent tendency has been for the incidence of acyanotic patients to be much higher. The technique of treating the stenosis has undergone changes in the course of years. Originally, closed operation involving the use of a valvotome and expanding dilator introduced through the outflow tract was adequate and the results reasonably good (7 deaths in 114 cases), but the later tendency has been towards open valvotomy through the pulmonary artery, commonly obtained by the use of hypothermia or heart-lung bypass (5 deaths in 84 cases). It has been observed that even after an apparently completely successful valvotomy the right ventricular pressure may not fall as much as would be expected, and emphasis is laid on the secondary changes that may occur in the hypertrophy of the infundibular region and the means by which this may produce functional stenosis. It has on occasions been recommended that infundibular resection should be performed in addition to the valvotomy in cases in which the right ventricular pressure remains high, but this procedure, involving incision and trauma to the right ventricle, may lead to serious cardiac weakness and the author's current policy is not to perform a routine infundibular resection in these cases.

The final section of the paper deals with the myocardial factor. There is little doubt that myocardial damage increases with the severity of the stenosis and duration of the disease, and the logical deduction is that in cases in which valvular stenosis is significant surgery at the earliest reasonable opportunity is clearly to be considered. *T. Holmes Sellors*

1434. **Repair of Ventricular Septal Defect in Infancy**
J. W. KIRKLIN and J. W. DUSHANE. *Pediatrics* [*Pediatrics*] **27**, 961–966, June, 1961. 3 figs., 5 refs.

In this report from the Mayo Clinic all cases of ventricular septal defect in children under the age of 2 years that have been operated on up to October, 1960, are reviewed, a total of 65. Operation was undertaken when there was recurrent or intractable congestive heart failure, when there was failure to thrive, or when the pulmonary hypertension was severe and was thought likely to increase still further. The pulmonary hypertension was mild (45% or less of the systemic pressure) in 7, moderate (45% to 75% of systemic pressure) in 17, and severe (75% or more of systemic pressure) in 41 cases. The operative technique was the same as that described previously (Kirklin *et al.*, *J. thorac. cardiovasc. Surg.*, 1960, **40**, 763; *Abstr. Wld Med.*, 1961, **30**, 118). Cardiac asystole has been used regularly and during the last 2 years has been produced by anoxic arrest, usually with normothermia. During the last 2 years halothane has been used as the anaesthetic agent, a median sternotomy has been employed, and all defects have been closed by direct suture without the use of a prosthesis.

The hospital mortality decreased from 67% in 1956 to 6% in 1959. In 1955 and 1956 the majority of the deaths were considered to be due to syndromes resulting from imperfect perfusion. Great attention to detail in pre- and postoperative care and management of perfusion is essential in these cases. Preoperative digitalization is employed and in the last 3 years a tracheostomy has been performed on only one patient. The high mortality of untreated ventricular septal defect in this age group is emphasized, but operation should be postponed until about 4 years of age if intensive medical measures produce a satisfactory improvement in the general condition. *R. L. Hurt*

1435. **The Surgical Treatment of Ventricular Septal Defect in Infancy. The Technic and Results of Pulmonary Artery Constriction**
A. G. MORROW and N. S. BRAUNWALD. *Circulation* [*Circulation*] **24**, 34–40, July, 1961. 7 figs., 12 refs.

Writing from the National Heart Institute, Bethesda, Maryland, the authors review briefly the results of attempts at full correction of ventricular septal defects in children under the age of 4 years and stress the high mortality in this age group (39 and 70% respectively in 2 series quoted). They also point out that although the lesion may be regarded as one of the more benign congenital cardiac defects a certain number of cases occur in which the high pulmonary arterial pressure and excessive pulmonary blood flow make it essential to attempt palliation before pulmonary resistance becomes too high. They have therefore tried to solve this problem by using a modification of the method of partial ligation of the pulmonary artery proposed by Muller and Dammann (*Surg. Gynec. Obstet.*, 1952, **95**, 213; *Abstr. Wld Med.*, 1953, **13**, 38). In this a nylon tape 1 cm. in width is gradually tightened around the pulmonary artery until a vigorous thrill is palpable distal to it. The tape is then further tightened until the mean pressure in the pulmonary artery is about 20 to 30 mm. Hg, when it is sutured in place. This procedure often entails constricting the artery to about one-third of its previous size.

Among 13 children aged from 3 to 22 months who were so treated there was only one death. Of the remaining 12, who have been followed for periods up to 4 years, all but one has shown considerable increase in growth and in exercise tolerance. The authors point out that the operation is essentially palliative, but that complete correction of the defect will be possible, and with a much lower mortality, when the infants have reached more mature years. *J. R. Belcher*

1436. **Treatment of Complete Transposition of the Great Vessels with the Blalock–Hanlon Operation**
J. L. OCHSNER, D. A. COOLEY, L. C. HARRIS, and D. G. MCNAMARA. *Circulation* [*Circulation*] **24**, 51–57, July, 1961. 2 figs., 19 refs.

Transposition of the great vessels is the fourth commonest congenital cardiac anomaly and is a potent cause of early death. Many methods aimed at palliation or correction of the condition have been described, but the

results have been far from satisfactory. In this paper the authors report from Baylor University School of Medicine, Houston, Texas, the results of attempted palliation by the creation of an atrial septal defect, following the technique of Blalock and Hanlon (*Surg. Gynec. Obstet.*, 1950, **90**, 1; *Abstr. Wld Surg.*, 1950, **8**, 62). They point out that for a child with this abnormality to survive at all there must be an intracardiac shunt of some sort to permit of at least partial oxygenation of the blood. Of a series of 64 such infants coming to necropsy at Texas Children's Hospital, 25 had a patent foramen ovale, but the commonest anomaly was a ventricular septal defect, only 6 having a true atrial septal defect.

Of the 45 patients operated on since 1955, in whom part of the intra-atrial septum was excised, 33 were between the ages of one day and one year, while 5 were aged 1 to 2 and 7 over 2 years; males preponderated in the proportion of 33 to 12. All were cyanosed and some also had congestive cardiac failure. The over-all operative mortality was 29% (13 deaths) and a further 2 patients died 2 and 9 months later respectively, but in the last 3 years the operative mortality has been greatly reduced (5 out of 28 patients or 18%). The majority of the survivors were significantly and often strikingly improved. The authors consider that although this is necessarily only a palliative procedure, the results justify it, and note that its operative mortality is much lower than that when complete correction is attempted. *J. R. Belcher*

1437. **Complete Correction of Tetralogy of Fallot: Use of the Combination of Cardiopulmonary Bypass and Deep Hypothermia**

F. Gerbode, J. B. Johnston, A. A. Sader, W. J. Kerth, and J. J. Osborn. *Archives of Surgery* [*Arch. Surg.*] **82**, 793–800, June, 1961. 5 figs., 5 refs.

The authors review their experience of 66 cases of tetralogy of Fallot treated by cardiopulmonary bypass at the Presbyterian Medical Center, San Francisco, with particular attention to the causes of death in the 23 fatal cases.

Of the 4 abnormalities originally described by Fallot, the significant defects are the patent interventricular septum and the obstruction to the right ventricular outflow, which become important clinically when they permit equal pressures in right and left ventricles and the septal orifice is greater than 1 cm. in diameter. In 59 of the authors' series the septal defect measured 2 cm. or more. Of the 66 cases, 38 were classified as cyanotic and 28 as acyanotic.

The operative procedure, using a rotating disk oxygenator and systemic hypothermia between 20° and 24° C. reinforced by local myocardial cooling with Ringer lactate solution at 0° C. and careful control of blood *p*H (Edmark technique), is fully and clearly described.

In making a critical analysis of postoperative mortality the cyanotic and acyanotic cases are considered separately. Of the 38 cyanotic patients, 15 died. (But only 5 of 20 cases ended fatally after the introduction of hypothermia.) The causes of death in these cases were: outflow tract too small, 3 cases; venous filling pressure kept too low, 2; residual auricular septal defect, 1; digitalis intoxication, 1; ventricular fibrillation during postoperative catheterization, 1; infection, 1; uncontrollable postoperative bleeding, 1; uncontrolled cardiac failure, 1; unknown, 4. In the acyanotic group 8 of the 28 patients died, the causes being as follows: outflow tract too narrow, 3 cases; myocardial damage by potassium, 1; haemorrhage, 1; ? heart block, 1; unknown, 2. In this group the significant cause of death was a preoperative pulmonary arterial pressure exceeding 40 mm. Hg. Where previous surgery—a Blalock or Potts operation—had been performed there appeared to be no hazard. The incidence of heart block was low (4 cases only). The surviving patients in both groups have all done well.

[This paper contains such a wealth of experience that it should be read in full.] *C. A. Jackson*

VALVULAR DISEASE

1438. **Chronic Rheumatic Heart Disease in Relation to Acute Rheumatic Fever.** (Les cardiopathies rhumatismales chroniques et leurs relations avec l'état rhumatismal aigu)

P. Isorni, J. Benevent, M. Foucher, and J. Gillet. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **54**, 501–510, May, 1961. 2 refs.

The authors have reviewed the histories of 114 cases of chronic rheumatic heart disease admitted over a period of 2½ years to the Hôpital de Versailles, Seine et Oise, in order to determine (1) whether there were any links between this condition and the acute articular rheumatism of childhood, and (2) the relation of febrile episodes in chronic rheumatic heart disease with acute rheumatic fever. Of these patients 101, mostly over 16 years of age, had mitral stenosis, associated in some cases with mitral incompetence or aortic or tricuspid valvular disease. There was a previous history of acute rheumatic fever in 53 only. For comparison, 74 patients, all except 2 under the age of 15 years, admitted over the same period for acute rheumatic fever were reviewed. These patients showed no evidence of established valvular disease, but 53 manifested myocardial involvement in the form of apical systolic murmurs and electrocardiographic changes.

Febrile episodes occurred in 69 patients with mitral disease, resembling in 45 an attenuated form of acute articular rheumatism, but only 5 had a sore throat and raised antistreptolysin titre. In 18 of the remaining patients over the age of 30 the pyrexia was of a different type and was uninfluenced by cortisone derivatives. The authors conclude that the existence of a link between acute rheumatic carditis and the onset of chronic rheumatic heart disease is doubtful. Acute rheumatism does not influence the course of the chronic disease, each appearing independently of the other; the difference is further demonstrated by the different effects of cortisone therapy, the different age incidence of the patients, and the ultimate course of acute rheumatic cardiopathy.

I. Ansell

1439. **Coronary Embolism and Angina in Mitral Stenosis**
C. OAKLEY, R. YUSUF, and A. HOLLMAN. *British Heart Journal* [*Brit. Heart J.*] **23**, 357–369, July, 1961. 8 figs., 14 refs.

This paper from Hammersmith Hospital (Postgraduate Medical School of London) reports 5 cases in which patients with mitral stenosis suffered coronary embolism resulting in cardiac infarction. In view of this occurrence a special study was made of 194 patients (152 women and 42 men) with dominant mitral stenosis in order to determine the incidence of coronary embolism and of ischaemic cardiac pain. Cardiac ischaemia was diagnosed on the finding of any one of the following features: angina of effort or a history of previous myocardial infarction; a positive electrocardiogram (ECG) after an exercise test in patients not receiving digitalis; ECG changes not attributable to ventricular hypertrophy, administration of digitalis, or hypokalaemia; or the finding at operation or necropsy of coronary arterial disease or a myocardial scar.

It was found that 42 (21·6%) of the patients suffered from angina of effort. Most of the patients with angina gave a positive effort test result and most of those without angina a negative result whether they were taking digitalis or not. Three possible causes of myocardial ischaemia were considered. (1) A low cardiac output; while this tended to be lower in those with angina, there was a wide scatter of results and the mean pulmonary vascular resistance was the same in both groups. (2) Occlusive coronary atherosclerosis; this might account for the ischaemia in some of the older patients, but since angina occurred in 16% of the patients under 40, most of whom were women, it was concluded that coronary arterial disease could account for only a small proportion of the cases. (3) Coronary occlusion due to embolism; in view of the course of events in the cases described it is considered that the cause of angina pectoris in mitral stenosis is not infrequently unsuspected coronary embolism and that this may be less rare than has been commonly supposed. *C. Bruce Perry*

CORONARY DISEASE AND MYOCARDIAL INFARCTION

1440. **Acute and Subacute Coronary Insufficiency**
P. WOOD. *British Medical Journal* [*Brit. med. J.*] **1**, 1779–1782, June 24, 1961. 1 fig., 7 refs.

This study, in which insufficiency is defined as that state in which the coronary circulation is insufficient to meet the full metabolic demands of the myocardium at rest, yet sufficient to prevent myocardial infarction, is based on 150 cases observed at the Brompton and National Heart Hospitals, London, and in private practice over a period of about 10 years. The illness was acute, that is, lasted less than 6 weeks, in 50% of the patients, subacute (2 to 6 months) in 45%, and chronic (longer than 6 months) in 5%. In most cases an attack of angina was witnessed and in many an electrocardiogram (ECG) was recorded during the attack. The average age of the patients was 56 and the male:female ratio was just under 3:1. Previous infarction had occurred in 25%. The ECG provided proof of ischaemic heart disease in 87%.

Clinical findings support the view that acute coronary insufficiency is due to coronary thrombosis without infarction, whereas patients in whom angina of effort deteriorates gradually to a state of angina at rest are suffering from progressive atherosclerosis. The most characteristic and diagnostic ECG change, which was seen in 80% of the series, is widespread ischaemic depression of the S–T segment at rest. Among 50 of the patients who were treated conservatively with rest, a low-calorie and low-fat diet, trinitrin tablets, and pentaerythritol tetranitrate the mortality was 30%. In contrast among 100 cases treated with anticoagulants in addition to the above measures the mortality was only 6%. When the trend towards this difference became obvious anticoagulants were withheld only when there was some definite contraindication to their use, such as a recent history of peptic ulcer, haematemesis, or jaundice, or geographical remoteness. Thus, the author notes, the last 30 patients in the control group were not chosen strictly at random. *G. S. Crockett*

1441. **Factors of Risk in the Development of Coronary Heart Disease—Six-year Follow-up Experience. The Framingham Study**
W. B. KANNEL, T. R. DAWBER, A. KAGAN, N. REVOTSKIE, and J. STOKES III. *Annals of Internal Medicine* [*Ann. intern. Med.*] **55**, 33–50, July, 1961. 2 figs., 13 refs.

In this paper are described the results of a 6-year survey of the development of coronary heart disease (C.H.D.) among a sample population in the town of Framingham, Massachusetts. The survey covered 4,469 persons aged 30 to 59 who came in for examination out of 6,507 selected; 740 volunteers were also included, making a total of 5,209. The criteria for the classification of C.H.D. followed those of the New York Heart Association.

Angina pectoris was diagnosed if two observers agreed that a patient experienced substernal discomfort of brief duration definitely related to exertion or emotion. Acute myocardial infarction was diagnosed on the electrocardiographic (ECG) findings if there was S–T segment elevation with late inversion of T waves and loss of initial QRS potentials. Old myocardial infarction was diagnosed on ECG grounds if there was loss of an R wave in leads where it would be expected or was previously present or if there was a Q wave of 4/100ths of a second duration or greater. Deaths which occurred in a matter of minutes and which could not be attributed to other causes by the physician in charge were regarded as being due to C.H.D.

Of the original 5,209 persons, 5,127 were accepted as free from C.H.D. and admitted to the study. Of these, 87% were examined at the fourth biennial review or later and another 2·4% were known to have died in the 6 years of follow-up. There was an over-all 6-year incidence of new cases of C.H.D. of 36·3 per 1,000 in the age groups studied, made up of 54·8 per 1,000 men

and 21·4 per 1,000 women. In the under-45 age group this sex difference was even greater, the incidence being 24·9 per 1,000 men and 1·9 per 1,000 women. The risk of developing C.H.D. was graded against serum cholesterol values and was found to be 3 times higher for those with a serum cholesterol level exceeding 244 mg. per 100 ml. than for those with a level below 210 mg. per 100 ml. A 2·6-fold increase in incidence of C.H.D. was found among men aged 40 to 59 with a raised blood pressure, and an even greater increase if there were ECG changes suggesting left ventricular hypertrophy. At each level of blood pressure the presence of ECG changes of left ventricular hypertrophy was associated with a 2- to 3-fold greater risk of C.H.D.

A marked sex difference in the way C.H.D. presented was noted; in 70% of the females the disease was manifested as angina pectoris, whereas only 30% of the males had this symptom. Most of the men who developed C.H.D. either had myocardial infarction or died suddenly; in two-thirds of the cases of sudden death in men this was the first manifestation of C.H.D.

C. T. Dollery

1442. **Prophylactic Quinidine after Myocardial Infarction**
T. B. Begg. *British Heart Journal* [*Brit. Heart J.*] **23**, 415–420, July, 1961. 12 refs.

The value of quinidine in preventing arrhythmias and sudden death after myocardial infarction was examined in a series of patients admitted to the Royal Victoria Infirmary, Newcastle upon Tyne. Seventy patients were included and were divided at random on admission into 2 groups, quinidine-treated and control. The distribution of patients between the two groups was uneven because a further 71 patients at first admitted to the trial were rejected from the final analysis, which was confined to patients with proven infarction who received anticoagulants for 3 weeks or died before that time. In 26 cases (19 men and 7 women) quinidine sulphate 0·3 g. (5 grains) 6-hourly by mouth was prescribed, beginning immediately and continuing in survivors for 21 days; and in 44 (31 men and 13 women) the drug was withheld. All patients were examined daily.

An arrhythmia, ventricular tachycardia which proved fatal, was observed in one of the 26 treated patients. Three members of the control group developed an arrhythmia, and to these may be added 2 other patients who were at first in the control group but were later rejected from it on being prescribed quinidine. Atrial fibrillation was observed in 3 of these 5 cases, partial or complete heart block in one, and atrial flutter in one. Seven (26·9%) of the quinidine-treated patients died within the 3-week observation period and 12 (27·3%) of the controls. Three of the former and 9 of the latter deaths occurred suddenly or during an attack of arrhythmia. Quinidine was found to be no more effective in patients under 60 than in those over that age, neither was it more effective in good-risk cases than in bad-risk cases.

This trial, it is concluded, gave no evidence that the routine administration of quinidine reduces the mortality rate or the incidence of arrhythmia from myocardial infarction. *Eirian Williams*

1443. **Prophylactic Procaine Amide in Myocardial Infarction**
P. C. Reynell. *British Heart Journal* [*Brit. Heart J.*] **23**, 421–424, July, 1961. 7 refs.

The efficacy of prophylactic procainamide in patients with myocardial infarction was investigated in the Bradford A Group Hospitals. Two different dosage schedules were used, those patients selected (by the toss of a coin) for treatment receiving either 0·5 g. of procainamide 4 times a day by mouth from the end of the first week after infarction to the end of the fourth week or 1·0 g. 4 times a day for the first week after admission and 0·5 g. 4 times a day for a further week. The treated group consisted of 51 patients (42 males and 9 females) and the untreated control group of 55 (39 males and 16 females).

The drug was found not to reduce the mortality. In the treated group there were 4 sudden deaths and one from delayed shock, and in the control group 3 sudden deaths and 2 from delayed shock. *Eirian Williams*

BLOOD VESSELS

1444. **Coarctation of the Aorta in Older Patients**
F. T. I. Oey and J. A. Noordijk. *Thorax* [*Thorax*] **16**, 169–175, June, 1961. 8 figs., 11 refs.

The authors, working at the University Hospital, Leiden, Netherlands, have attempted to extend the known facts about the natural history of coarctation of the aorta, with particular reference to the surgery of the condition, by investigating 32 patients aged 35 or over who were operated on for correction of the lesion. It should be noted that only 11 patients were 40 years old or over, and none was over 50 with the exception of a man aged 52 who died a few days after the operation.

They conclude that there is "certainly an indication for operation in patients more than 35 years old, even if the coarctation of the aorta has not yet given rise to symptoms. The surgical risk in these patients is acceptable. The results obtained justify the hope that the expectation of life will improve as a result of the operation".

[The authors have not established their case because of an intrinsic error in their method of assessment of the natural history of disease. There has been no clinical study of old people living in their homes relating to the incidence of coarctation of the aorta. Certainly one has seen minor degrees of this condition in routine post-mortem examinations of extremely elderly subjects when the diagnosis had not been made in life. This solitary appraisal of events occurring in a few middle-aged patients after operation will not add materially to our knowledge of whether to operate or not when the condition is giving rise to no symptoms or complications.]

P. D. Bedford

1445. **Surgical Treatment of Dissecting Aneurysm of the Aorta: Analysis of Seventy-two Cases**
M. E. De Bakey, W. S. Henly, D. A. Cooley, E. S. Crawford, and G. C. Morris Jr. *Circulation* [*Circulation*] **24**, 290–303, Aug., 1961. 12 figs., bibliography.

1446. **Hypertension after Resection of Coarctation of the Aorta**

C. J. Ingomar and E. Tersley. *British Heart Journal* [*Brit. Heart J.*] **23**, 370–376, July 1961. 3 figs., 15 refs.

During recent years it has been recognized that after an apparently successful operation for coarctation of the aorta the blood pressure may temporarily rise to above the preoperative level. The frequency of this " reactive " hypertension has been studied at the Rigshospital and Dronning Louises Children's Hospital, Copenhagen. Measurement of the blood pressure every 15 minutes after the operation showed that in 5 of 33 children (11 girls and 22 boys) there was a striking rise in blood pressure occurring within 24 hours in 4 and within 48 hours in one. All 5 were under 6 years of age and 3 were less than one year old. In the whole group 9 were aged under one year and the eldest was 14.

One of the patients showed postoperative haematuria (but no sign of renal damage was found at necropsy), in another there was postoperative albuminuria and gangrene of the ileum, and in a 3rd patient post-mortem examination showed renal infarction. It thus appears that the reactive hypertension may be renal in origin. It was not possible to establish any relationship between the length of time the aorta was occluded (this ranged from 20 to 70 minutes) and the occurrence of reactive hypertension. It is nevertheless recommended that, particularly in very young children, the period of occlusion of the aorta should be as short as possible. It is further recommended that the aortic clamps after performance of the anastomosis should be released very slowly in order to avoid any sudden rise in pressure in those regions, particularly around the kidneys, spleen, and intestine, previously subjected to hypotension.

C. Bruce Perry

1447. **The Use of an Environmental Temperature Vasomotor Test in the Evaluation of Peripheral Arterial Disease**

A. Ebel, O. A. Rose, and K. Raab. *Angiology* [*Angiology*] **12**, 310–315, July, 1961. 1 fig., 6 refs.

The authors describe their experience at the Veterans Administration Hospital, Bronx, New York, with the environmental temperature test introduced by Robertson and Smithwick (*Boston med. Quart.*, 1950, **1**, 8) for the evaluation of vasomotor activity in patients with peripheral arterial disease. It is performed in the following manner. The temperature in the examination room is adjusted to 68° F. (20° C.), the patient being fully undressed except for a towel across the lower abdomen and pelvis; the lights in the room are dimmed or extinguished to promote relaxation. At the end of one hour temperatures are recorded at the distal ends of all toes, the plantar surface of the feet, and at the level of the malleoli. The thermostatic control is then changed to 83° F. (28·3° C.) and as soon as the temperature in the room reaches this point timing of the warm phase of the test is begun; at the end of one hour skin temperatures are recorded as above. If the toe temperatures do not reach 90° F. (32·2° C.) or higher, the patient is kept in the warm environment for an additional hour, at the end of which skin temperatures are again recorded. If maximum vasodilatation is not achieved (toe temperatures of 90° F. or above) the test is repeated on a subsequent day, omitting, however, exposure to the cold room (68° F.), while some 15 to 20 minutes before the test the patient is given 200 mg. of quinalbarbitone sodium by mouth. (For young, female, or debilitated patients the dose is reduced to 100 mg.) Skin temperature readings are then taken as before at the end of one hour, or if necessary after 2 hours, and the patient thereafter returned to bed and kept under close observation.

The authors have found this test simple to perform, to have high reliability, and to be better tolerated by the patient than most similar methods in current use. They suggest that the part played by the higher cortical (" psychomotor ") centres in the control of peripheral vasomotor tone has been underestimated and conclude that " the fact that complete sedation was necessary for the complete release of vasoconstriction suggests that the psychomotor factor may well be responsible for the many instances of failure with the usual vasodilator tests ".

Leon Gillis

HYPERTENSION

1448. **Studies of the Pathogenesis of Human Hypertension: the Adrenal Cortex and Renal Pressor Mechanism**

J. Genest, P. Biron, E. Koiw, W. Nowaczynski, R. Boucher, and M. Chrétien. *Annals of Internal Medicine* [*Ann. intern. Med.*] **55**, 12–28, July, 1961. 7 figs., 38 refs.

This paper from the Hôtel-Dieu de Montréal describes a study of the interrelationships between the adrenal cortex, the kidney, and human hypertension. Measurements in 142 hypertensive patients and normal subjects showed that the urinary excretion of aldosterone was increased in renal, essential, and malignant hypertension. There was considerable overlap between the normal and hypertensive groups, but part of this may be explained by the considerable fluctuations in daily urinary aldosterone excretion observed in patients studied serially. Associated with increased aldosterone excretion a highly significant decrease in urinary pregnanetriol was found.

Normal subjects infused with angiotensin for 3 to 14 hours showed a rise in blood pressure of 15 to 35 mm. Hg, a fall in glomerular filtration rate of 10 to 40%, and a 2½- to 11-fold increase in urinary aldosterone excretion; this was accompanied by sodium retention and a fall in the urinary sodium:potassium ratio. Angiotensin infusions at a slow rate insufficient to produce a rise in diastolic blood pressure also brought about a 2- to 3-fold increase in urinary aldosterone excretion in normal subjects. Hypertensive patients responded to angiotensin infusions with a similar increase in aldosterone excretion and rise in blood pressure, but in contrast there was an increase in urinary sodium excretion. A new method of assaying angiotensin in blood showed that some angiotensin is present in the blood of many hypertensive patients.

The aldosterone excretion results in patients with benign essential hypertension differ from those of Laragh

and colleagues (*J. clin. Invest.*, 1960, **39**, 1091; *Med. Clin. N. Amer.*, 1961, **45**, 321; *Abstr. Wld Med.*, 1961, **29**, 25), who found it normal; but both agree that aldosterone secretion is raised in malignant hypertension.

C. T. Dollery

1449. **The Effect of an Antithyroid Drug on the Clinical Course of Malignant Hypertension**
G. A. PERERA. *Annals of Internal Medicine* [*Ann. intern. Med.*] **55**, 29–32, July, 1961. 13 refs.

This paper from the Presbyterian Hospital, New York, reports the results of treating 4 patients with malignant hypertension with the antithyroid drug methimazole. All 4 had antecedent hypertension and later developed the clinical syndrome of proteinuria, high diastolic pressure, and papilloedema. The blood urea nitrogen concentration was less than 25 mg. per 100 ml. Two patients had no antihypertensive drugs and 2 received reserpine and hydrallazine, which were later stopped. All were rendered myxoedematous. The 2 patients treated with methimazole alone lost their headache and the retinopathy cleared over 3 months. The proteinuria and raised blood pressure persisted. One patient died suddenly after 3 months, while the other is alive and well 9 months later.

The 2 patients who were treated with antihypertensive drugs responded by a minimal decrease in blood pressure and remission of the exudative retinopathy and papilloedema. One of these patients was given a cough mixture containing iodide a year later and had a return of headaches and papilloedema.

[Although interesting, this study is unlikely to be imitated in view of the proved efficacy of antihypertensive drugs in controlling the syndrome of malignant hypertension and the disastrously rapid deterioration of kidney function that sometimes occurs when the high blood pressure is left untreated. Exudative retinopathy and papilloedema are the manifestations of malignant hypertension most sensitive to treatment, and the rice diet sometimes led to regression of retinopathy without change in blood pressure.] *C. T. Dollery*

1450. **Recent Experience of Long-term Treatment with Guanethidine and Its Combination with Cyclopenthiazide.** (Neuere Erfahrungen über die Langzeitbehandlung mit Guanethidin und dessen Kombination mit Cyclopenthiazid)
H. W. BUCHER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **91**, 914–918, Aug. 5, 1961. 3 figs., 10 refs.

Treatment with " ismelin " [guanethidine] was carried out on 11 patients for over a year. After an initial orthostatic hypotensive reaction the patients became adapted and were able to undergo long-term therapy without any complaints. Adaptation to the drug did not occur. Follow-up examination showed throughout an improvement in the ocular fundus together with maintenance or improvement of kidney function. The potentiating effect of saluretics, especially the new drug cyclopenthiazide (" navidrex "), which causes practically no fall in the blood potassium level, is again emphasized. Because of its negligible side-effects ismelin is considered to be one of the best drugs now available for long-term therapy and one which will definitely improve the prognosis in severe forms of hypertension.—[From the author's summary.]

1451. **Further Experience with Guanethidine**
A. W. D. LEISHMAN, H. L. MATTHEWS, and A. J. SMITH. *Lancet* [*Lancet*] **2**, 4–7, July 1, 1961. 1 fig., 8 refs.

In this paper from the Sheffield Royal Infirmary the authors review their experience with guanethidine in the treatment of 114 hypertensive patients, most of whom received the drug for more than 11 months. Of 100 patients treated continuously with guanethidine, 67 had a reduction in their standing diastolic pressure of 30 mm. Hg or more and were judged to be well controlled. The range of dose required was 10 to 150 mg. daily, although most patients were controlled with 20 to 60 mg. daily. Twenty patients required one or more increases in dose to maintain control of blood pressure. Symptoms of hypotension occurred frequently and 6 patients had transient cerebral ischaemia during such episodes. Diarrhoea, muscle weakness, and fluid retention were the main side-effects encountered.

The authors conclude that guanethidine is suitable for the long-term treatment of hypertension and that tolerance is unlikely to be a serious problem, although it occurs to a moderate extent in about 1 in 5 patients.

[An indication of the severity of the hypertension in the patients treated would have facilitated comparison with experience in other centres.] *C. T. Dollery*

1452. **Guanethidine in Treatment of Hypertension**
G. E. BAUER, F. J. T. CROLL, R. B. GOLDRICK, D. JEREMY, J. RAFTOS, H. M. WHYTE, and A. A. YOUNG. *British Medical Journal* [*Brit. med. J.*] **2**, 410–415, Aug. 12, 1961. 17 refs.

In this report from the Cardiovascular Clinic, Sydney Hospital, Australia, the authors describe experience with guanethidine in the treatment of 28 patients with hypertension for periods ranging from 2 to 12 months. All the patients had a diastolic blood pressure greater than 100 mm. Hg before treatment, and in 4 the hypertension was in the malignant phase with papilloedema. Four patients had significant renal failure with blood urea nitrogen levels between 26 and 44 mg. per 100 ml. Most patients were treated as out-patients even during the initial stabilization period. The starting dose was 10 or 12·5 mg. once daily, and this dose was increased by increments of 12·5 mg. at weekly intervals to a maximum of 75 mg. daily. In addition, 23 patients received either an oral diuretic or reserpine, or both these in combination.

Some reduction in blood pressure was achieved in all cases, and in 18 this was regarded as good—that is, a pressure below 150/100 mm. Hg in the standing posture. Drug tolerance was not a problem. Side-effects were mainly slight and similar to those reported by other authors (bradycardia, urgency of defaecation, nasal stuffiness, failure of ejaculation). In addition, 4 patients developed depressive symptoms which were thought to

be precipitated by guanethidine; one patient committed suicide.

The authors emphasize the slow and cumulative effect of the drug, which necessitates caution in the regulation of dosage. They compare its action with that of bretylium and conclude that guanethidine is the more suitable drug for routine clinical use. *M. Harington*

1453. **Methoserpidine: a Non-depressant Isomer of Reserpine**
M. C. Holt. *British Medical Journal* [*Brit. med. J.*] 2, 415–418, Aug. 12, 1961. 14 refs.

Methoserpidine ("decaserpyl"; 10-methoxydeserpidine) is an alkaloid of the rauwolfia group, an isomer of reserpine, which is prepared synthetically. From the results of animal and clinical trials several workers have suggested that this drug retains the antihypertensive potency of reserpine, but is relatively free from undesirable effects on the central nervous system, particularly depression. In this report the author describes a trial of methoserpidine in a series of hypertensive patients who attended the Royal Eye Hospital, London, with ocular symptoms and were referred for a physician's opinion. The trial was conducted on an out-patient basis, and 30 consecutive patients with non-malignant hypertension were included. There was a considerable number of elderly patients, the youngest being 44 and the average age 64 years. No placebo tablets were used in view of the high incidence of acute retinal vascular lesions among the patients. Treatment was started with 15 to 30 mg. of methoserpidine daily divided into 3 equal doses. The maintenance dosage was found to vary from 5 to 80 mg. daily. The patients attended weekly, and the effect of treatment was assessed from repeated casual measurements of the blood pressure by the author and by specific questioning about side-effects. The average period of observation was 5½ months.

The results show that under the conditions of this trial 20 of the 30 patients had a good hypotensive response as judged by a fall in diastolic blood pressure of over 20 mm. Hg, the final level being below 100 mm. Hg. The proportion of patients responding was very similar to that found by the author in a control series of patients previously treated with reserpine in the same clinic and suggests that the antihypertensive activity of the two drugs is comparable. Side-effects were infrequent and usually mild; nasal stuffiness occurred in 3 cases and some drowsiness or fatigue in 5 (mostly on larger doses, that is, 60 mg. daily). In 2 patients treatment had to be stopped on account of muzziness in the head or headache; 2 patients developed depression, but this was not severe enough to necessitate stopping the drug.

The author concludes that her results bear out the original claims that methoserpidine is as effective a hypotensive agent as reserpine, but with less risk of causing depression. *M. Harington*

1454. **Thyroid Treatment of Essential Hypertension—the Importance of Early Diagnosis**
P. Menof. *South African Medical Journal* [*S. Afr. med. J.*] 35, 790–795, Sept. 23, 1961. 5 figs., 25 refs.

1455. **Incidence of Hypokalaemia in Severe Hypertension**
O. Wrong. *British Medical Journal* [*Brit. med. J.*] 2, 419–421, Aug. 12, 1961. 1 fig., 18 refs.

The author reports a survey of the incidence of hypokalaemia in patients with severe hypertension seen at University College Hospital, London. All 64 patients studied had a diastolic blood pressure of 120 mm. Hg or higher on admission to hospital, and 14 of them had papilloedema. Patients with diarrhoea, vomiting, congestive heart failure, or severe renal failure were excluded from the survey, as also were those receiving corticosteroids, diuretics, or effective antihypertensive treatment.

The results confirm the finding of previous investigators that plasma potassium levels are not infrequently low in severe hypertension. In the author's series 13 (20%) of the 64 patients had a plasma potassium level below 3·5 mEq. per litre, and the incidence was greater (43%) in those with papilloedema. Many of the patients with hypokalaemia also had alkalosis. None suffered from muscular paralysis, but the majority of the hypokalaemic patients had nocturia, and a history of this latter symptom was found to be of help in predicting whether a hypertensive patient might have hypokalaemia.

The 13 patients with hypokalaemia were fully investigated as to the aetiology of their hypertension. Nine were found to have a possible renal cause for hypertension, and 5 had renal ischaemia on one or both sides. In none was primary hyperaldosteronism thought to be present. The author concludes that the hypokalaemia of severe hypertension is probably due to secondary hyperaldosteronism, which in turn is caused by renal ischaemia or perhaps by the severe hypertension itself.
M. Harington

1456. **Renal Arteriography and Differential Renal Function Tests in the Diagnosis of Unilateral Renal Hypertension**
I. M. Breckenridge, D. A. E. Dewar, D. M. Douglas, K. G. Lowe, and H. G. Morgan. *Scottish Medical Journal* [*Scot. med. J.*] 6, 295–300, July, 1961. 6 figs., 6 refs.

The authors describe in detail 2 cases of hypertension due to unilateral kidney disease admitted to the Royal Infirmary, Dundee, in which cure followed nephrectomy. Both patients were young—one a 29-year-old woman and the other a 26-year-old man—and the onset of hypertension was recent, normal blood pressure having been noted in both cases up to approximately 2 years before their admission to hospital.

Pyelography revealed a difference in size between the two kidneys in both cases. Differential renal function tests were then carried out, and these showed decreased sodium excretion rates from the smaller kidney as well as decreased total flow rates. Aortography revealed stenosis of the renal artery with post-stenotic dilatation in the female patient and abrupt termination of the vessel in the man, and these findings were confirmed at operation. The authors discuss their reasons for carrying out both aortography and differential renal function tests before proceeding to operation.
H. F. Reichenfeld

Clinical Haematology

1457. **Therapy of Hypoplastic Anemia with Bone Marrow Transplantation**
W. McFarland, N. Granville, R. Schwartz, H. Oliner, D. K. Misra, and W. Dameshek. *Archives of Internal Medicine* [*Arch. intern. Med.*] **108**, 23–33, July, 1961. 3 figs., 27 refs.

At the Pratt Diagnostic Clinic–New England Center Hospital, Boston, 37 cases of hypoplastic anaemia were observed over a period of 3 to 5 years. All patients had severe pancytopenia, hypoplasia of the bone marrow, and absence of splenomegaly and other underlying disease. Twenty patients were treated with bone-marrow infusions and 17 served as controls.

In the control group all the 17 patients were given blood transfusions, 3 underwent splenectomy, and 15 received corticosteroids. After a period ranging from 3 to 5 years 6 of the 17 are alive and 11 are dead, none having died of infection. The survivors are clinically well and require the minimum of medical attention, although varying degrees of haematological abnormality persist in most cases. The 20 patients who received bone-marrow transplantation were also treated with blood transfusions and all were given corticosteroids. Splenectomy was performed in 11 cases. After a follow-up of one to 3 years 9 are alive and 11 are dead, 4 of this group dying of infection.

There was no significant difference between the two groups in terms of over-all survival. Splenectomy had no apparent effect in either group and there was no correlation between the dose of marrow cells received and the length of survival. Beneficial changes, however, followed bone-marrow infusions in 5 cases. Patients receiving marrow from related donors responded better than those who received marrow from unrelated donors. It is unlikely that prolonged " take " of marrow occurred. More exact data are particularly needed with respect to the value of actual, although temporary, bone-marrow transplantation, and the combined effects of marrow infusion and splenectomy. *A. W. H. Foxell*

1458. **Red-cell Production and Destruction in Myelosclerosis**
L. Szur and M. D. Smith. *British Journal of Haematology* [*Brit. J. Haemat.*] 7, 147–168, April, 1961. 10 figs., 47 refs.

At the Hammersmith Hospital and Postgraduate Medical School of London the authors studied the production and destruction of erythrocytes in 19 patients with a proved diagnosis of myelosclerosis, ^{51}Cr being used to assess erythrocyte survival and ^{59}Fe for the assessment of erythropoiesis. Both estimations of blood activity and surface-counting techniques were used. Erythrocyte survival was shortened in all except one of the patients, but the shortening was not so striking as that found in haemolytic anaemia; with the exception of the one normal patient the mean cell life varied from 25 to 59 days and was less than 20 days in only 4 patients. The authors consider that this shortening indicates " ineffective " erythrocyte formation. Surface counting over the spleen showed mostly an accumulation of radioactivity that was within or just over the normal limits; in 4 patients, however, there was evidence of considerably excessive accumulation.

In the studies with ^{59}Fe the iron turnover and the erythrocyte utilization of iron were estimated and surface counting was carried out over the spleen, liver, heart, and sacrum. All but 2 of the patients showed increased plasma iron turnover, while in 9 of the 16 studied erythrocyte utilization of iron was considerably decreased. As judged by uptake of iron in the sacrum, erythropoietic marrow activity was decreased or absent. Extramedullary haematopoiesis in the spleen was evident in 11 patients, and 5 of these had evidence of erythropoiesis in the liver as well.

The results support the " compensation " theory—that is, that extramedullary haematopoiesis is an attempt to maintain erythrocyte and haemoglobin levels in the face of failing marrow function. Irradiation of the spleen was given to 5 patients because of the pain and discomfort from the enlarged spleen; treatment was limited to the lower half of the organ because all the patients had evidence of splenic erythropoiesis. Irradiation abolished erythropoiesis in the exposed areas and the patients' packed-cell volume and haemoglobin levels fell during the next 3 months, but their symptoms were much relieved. In the authors' opinion splenectomy should be considered only for patients who show (1) clear evidence of excessive erythrocyte destruction in the spleen, and (2) no evidence of haematopoiesis in the spleen. But the operation may need to be considered when only the first of these conditions is fulfilled if transfusion requirements are great owing to dominant haemolysis. *M. C. G. Israëls*

1459. **Some Aspects of the Pathology of Anaemia. I. Theory of Maturation Arrest. II. Investigation of Castle's Hypothesis.** [Lumleian Lecture]
L. J. Witts. *British Medical Journal* [*Brit. med. J.*] **2**, 325–328, Aug. 5, 1961, and 404–410, Aug. 12, 1961. 1 fig., bibliography

1460. **Iron Deficiency after Partial Gastrectomy**
J. R. Hobbs. *Gut* [*Gut*] **2**, 141–149, June, 1961. 4 figs., 41 refs.

This paper from the Central Middlesex Hospital, London, presents a review of the aetiology of iron deficiency after partial gastrectomy and the results of the author's treatment of patients in whom anaemia developed after partial gastrectomy. It was found that ferrous sulphate in a dosage of 3 tablets a day after

meals (equivalent to 215 mg. Fe daily) was inadequate for most patients with this type of anaemia. On the other hand ferrous glycine sulphate, 3 tablets a day between meals or one tablet at night (equivalent to 150 mg. or 50 mg. Fe), proved satisfactory after one month's treatment in the majority of cases. The rate of intolerance to ferrous sulphate tablets was between 8% and 20%, but no case of intolerance to ferrous glycine sulphate occurred.

It is therefore concluded that treatment with tablets of iron chelate—namely, ferrous glycine sulphate—or syrup of ferrous glycine sulphate is the optimum therapy for this type of anaemia; one tablet taken on lying down each night is adequate in the treatment of mild anaemia and prevents its recurrence. *I. McLean Baird*

1461. **Gastric Juice in Pernicious Anemia. Physicochemical Composition of Gastric Juice in Complete Achlorhydria and Composition of Primary Alkaline Secretion of the Stomach**

A. Lambling, J. J. Bernier, Y. Najean, and J. Badoz-Lambling. *American Journal of Digestive Diseases* [*Amer. J. dig. Dis.*] 6, 629–645, July, 1961. 9 figs., 38 refs.

In true pernicious anaemia (Biermer's disease) there is almost invariably an absence of gastric acid-secreting parietal cells. In all of 16 patients with proven pernicious anaemia examined at the Hôpital Bichat, Paris, histamine-fast achlorhydria (average total acidity 5·2 mEq. per litre) was demonstrated. The test was carried out by taking two initial samples of gastric juice and then a further 8 samples at 15-minute intervals after the intramuscular injection of 0·5 mg. of histamine dihydrochloride.

The authors have confirmed the presence also of an alkaline secretion produced by columnar or neck chief cells; these are unaffected in pernicious anaemia, so that the pure alkaline secretion can be measured " as a function of the quantity of 0·1 HCl " which will cause Töpfer's reagent to change colour, which occurs at *p*H 3·5. In pernicious anaemia the alkaline curve remains flat; evidence is presented that alkaline secretion in pernicious anaemia is comparable to that in a normal stomach (the average alkalinity was 39·2 mEq. per litre, with a wide scatter). The flat curve is due to the absence of acid secretion, so that no alkali is neutralized. This is true achlorhydria; it is characteristic of pernicious anaemia and is very rare in other conditions (among 73 non-anaemic achlorhydric patients examined true achlorhydria was found only in 5—3 with cirrhosis and 2 with early gastritis).

In relative or apparent achlorhydria not associated with pernicious anaemia there is a reduction in alkalinity during histamine stimulation; this is due to neutralization of part of the alkali by a small amount of residual acid secretion which, in the usual test, is obscured by neutralization. By determining the type of alkali curve the achlorhydria of true pernicious anaemia can be distinguished from other types of achlorhydria in some 80% of cases. During the test higher than normal contents of sodium and potassium ions were demonstrated, and lower than normal amounts of chloride ions; the only constituent of the gastric juice which altered on histamine stimulation was potassium, which decreased.

R. B. Thompson

1462. **Radioactive Vitamin B_{12} Absorption in the Megaloblastic Anaemia Caused by Anticonvulsant Drugs**

F. G. Lees. *Quarterly Journal of Medicine* [*Quart. J. Med.*] 30, 231–248, July, 1961. 8 figs., 27 refs.

The megaloblastic anaemia due to anticonvulsant drugs usually responds to treatment with folic acid. Previous studies, however, have indicated that there is no deficiency of folic acid but rather a failure of utilization. Estimates of serum vitamin-B_{12} levels and of absorption of the vitamin have also mostly given normal results, though occasionally low serum levels have been recorded. At Manchester Royal Infirmary the present author has studied 8 patients and estimated the vitamin-B_{12} absorption by the Schilling test when the patients were first seen with anaemia and again at varying intervals after treatment with folic acid. The methods are described.

In 7 of these 8 patients the absorption of vitamin B_{12} was considerably increased during folic acid therapy and in the remaining patient there was some slight increase. The patients all showed initial absorption levels above those usually found in pernicious anaemia. A control experiment showed that folic acid does not cause similar changes in patients who were not taking anticonvulsant drugs and had no evidence of anaemia or gastro-intestinal disease. The changes observed in the anaemic patients during folic acid therapy occurred whether the anticonvulsant drugs were withdrawn or not. Three patients showed a reticulocyte response to the vitamin B_{12} given during the Schilling test. The author concludes that the effect of anticonvulsant drugs is to cause a relatively defective absorption of vitamin B_{12} in the intestine, which can be overcome by folic acid therapy.

M. C. G. Israëls

1463. **Therapeutic Effect, Utilization, and Fate of Injected Vitamin B_{12} in Man: a Preliminary Report**

J. F. Adams. *British Medical Journal* [*Brit. med. J.*] 1, 1735–1737, June 17, 1961. 6 figs., 3 refs.

At the Western Infirmary, Glasgow, 6 patients with pernicious anaemia were given doses of labelled vitamin B_{12} (cyanocobalamin) so that the excretion of the vitamin could be studied, and vitamin-B_{12} levels were followed for some weeks, the *Euglena* method of estimation being used. The results show that a dose of 1,000 μg. does not prolong the rise in the serum vitamin-B_{12} level very much more than a dose of 100 μg., and even the maximum serum level of vitamin B_{12} reached may not be very different with the two doses. This effect does not appear to be due to excretion of the excess when the 1,000-μg. dose is given, and no firm explanation has so far been found. In practice this means that doses of 1,000 μg. of vitamin B_{12} for the maintenance treatment of pernicious anaemia are unnecessary; just as good an effect can be obtained with 100 μg. and, judged by the serum vitamin-B_{12} levels, one dose every 3 to 5 weeks seems to be adequate.

M. C. G. Israëls

NEOPLASTIC DISEASES

1464. **The Delayed Skin Test Response in Hodgkin's Disease and Lymphosarcoma: Effect of Disease Activity**
J. E. Sokal and N. Primikirios. *Cancer* [*Cancer (Philad.)*] **14**, 597–607, May–June, 1961. 32 refs.

The occurrence in Hodgkin's disease and some related conditions of skin unresponsiveness to tuberculin antigen and other antigens is now well known. In this study reported from the Roswell Park Memorial Institute, Buffalo, New York, patients with Hodgkin's disease, lymphosarcoma, and chronic lymphocytic leukaemia were tested by intradermal injection of tuberculin (P.P.D.), an extract of various species of *Trichophyton*, and an extract of *Candida albicans*; hospital patients with other diseases and healthy individuals served as controls. P.P.D. was used in two different strengths, and the response of both patients and controls to B.C.G. vaccination was also tested. The patients with Hodgkin's disease, lymphosarcoma, and chronic lymphocytic leukaemia were divided into two categories according to the presence or absence of systemic manifestations. In 34 patients with these diseases tuberculin tests were repeated at intervals of several months, the disease activity being assessed and recorded before testing.

The patients with Hodgkin's disease, lymphosarcoma, and chronic lymphocytic leukaemia showed depression of skin reactivity which could be correlated with the activity of the disease. This anergy was most marked in the patients with Hodgkin's disease, who were often found to be anergic even when symptom-free. The skin reactions in patients with lymphosarcoma and chronic lymphocytic leukaemia when asymptomatic were not clearly distinguished from those in the controls. Skin anergy, where it occurs, appears to be relative rather than absolute, and some patients who did not react to tuberculin did so on retesting after B.C.G. vaccination. These results have shown that skin reactivity fluctuates with activity of the disease; thus some patients who failed to react in relapse reacted in therapeutically induced remissions. The evidence obtained from this and other studies suggests that depression of delayed skin responses in Hodgkin's disease and related conditions is a consequence of the disease and not an antecedent factor. The authors conclude that in Hodgkin's disease, and to a lesser extent in the other two diseases investigated, there is an unidentified defect of certain cellular immune reactions. *A. G. Baikie*

1465. **Cytogenic Studies in Acute Leukaemia**
A. G. Baikie, P. A. Jacobs, J. A. McBride, and I. M. Tough. *British Medical Journal* [*Brit. med. J.*] **1**, 1564–1571, June 3, 1961. 1 fig., 19 refs.

Of 31 cases of acute leukaemia in adults studied at the Western General Hospital, Edinburgh, chromosome studies were possible in 22; these were carried out on the bone marrow in 8 cases, on the peripheral blood in 7, and on both in 7. The technique of Ford *et al.* (*Nature (Lond.)*, 1958, **181**, 1965) was used for the marrow studies and a modification of that of Moorhead *et al.* (*Exp. Cell Res.*, 1960, **20**, 613) for the peripheral blood. Five cases had been mentioned in an earlier report (Baikie *et al.*, *Lancet*, 1959, **2**, 425; *Abstr. Wld Med.*, 1960, **27**, 334). Possible sampling errors are commented upon—the marrow and peripheral blood findings may differ—and other technical difficulties are discussed; for instance, the possibility that normal cells may outgrow leukaemic cells in culture. It is felt that the incidence of abnormalities is probably underestimated; 30 cells is regarded as the minimum which must be examined for the chromosome distribution to be assessed.

In 8 patients abnormalities were found. Five had abnormal chromosome count distributions and 2 had morphological abnormalities, while in one case a few cells had 51 chromosomes and a chromosome fragment. The very variable chromosomal abnormalities reported in acute leukaemia contrast with the apparently specific abnormality found in chronic myeloid leukaemia; this is never seen in acute leukaemia unless there has been acute blastic transformation in a patient with chronic myeloid leukaemia. Abnormalities are more likely to be found in those cases of acute leukaemia which have been induced by radiation and in those with a low peripheral leucocyte count. *R. B. Thompson*

1466. **The Skeletal Lesions of Acute Leukemia**
L. B. Thomas, C. E. Forkner Jr., E. Frei III, B. E. Besse Jr., and J. R. Stabenau. *Cancer* [*Cancer (Philad.)*] **14**, 608–621, May–June, 1961. 12 figs., 41 refs.

At the Clinical Center of the National Institutes of Health, Bethesda, Maryland, 85 patients with acute leukaemia were classified according to age, sex, and leukaemic cell type. Radiological examination of the skeleton was carried out on admission, and certain bones were re-examined at intervals without regard to signs or symptoms of the leukaemia. At necropsy, in 53 out of 74 cases, one femur with the knee joint and the proximal portions of the tibia and fibula were removed for detailed study including histological examination. In the 41 children in the series the effects of the disorder on growth were studied.

In children with acute leukaemia pain in the bones tends to occur in the extremities and is due to leukaemic cell infiltration of the periosteum. In adults bone pains are more commonly central and are due to osteolytic lesions or osteoporosis. Infarction of bone occurred terminally in about one-third of the patients studied. When acute leukaemia was active in children bone growth was found to be impaired, but normal or even accelerated growth was restored during remissions. Radiological evidence of bone lesions was much more frequent in children than in adults. The more common abnormalities at all ages were juxta-epiphysial radiotranslucent bands, osteoporosis, osteolytic lesions, cortical or periosteal defects, and the occurrence of lines marking arrest of growth. Clinically, arthritis occurred in 14% of patients and was invariably associated with fever. The arthritis is probably due to cortical lesions or to leukaemic cellular infiltration of the periosteum adjacent to the joint capsule. The occurrence and severity of bone lesions was not obviously related to sex or leukaemic cell type. *A. G. Baikie*

Respiratory System

1467. **The Treatment of Chronic Tonsillitis.** (К вопросу о лечении хронического тонзиллита)
T. V. Boltunova, I. G. Aržanova, and O. G. Bolotova. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **6**, 16–18, June, 1961.

The conservative treatment of chronic tonsillitis in children, especially in those with rheumatism, is becoming accepted by more and more clinicians. The subjection of a child to tonsillectomy is a procedure not to be undertaken without grave reason, involving as it does psychic trauma and the removal of tissues which, when healthy, serve as a barrier to infection. There have been reports of good results from electrophoresis with procaine, and the present authors report the results in a series of 30 children so treated. The procedure is usually well tolerated, although 3 children had exacerbations during treatment which necessitated its interruption for a few days, after which the course of 25 to 30 applications was resumed with good effect.

As a result of the treatment the general health of the children improved, attacks of tonsillitis became rarer—in 20 cases they were absent for 6 to 12 months—and the children were able to take part in bathing and other sports and pastimes without the fear of recurrences. The tonsils became smaller and healthier, showing no pus in the lacunae and other signs of infection, while the erythrocyte sedimentation rate and haemoglobin value became normal. The authors recommend that this simple and innocuous treatment be given a full trial before tonsillectomy is resorted to.

[A 2% solution of procaine is referred to in the summary, but no details of strength of solution or duration of applications are given in the body of the paper.]

L. Firman-Edwards

LUNGS AND BRONCHI

1468. **Pulmonary Embolism: a Clinical and Pathologic Study with Emphasis on the Effect of Prophylactic Therapy with Anticoagulants**
R. E. Hermann, J. H. Davis, and W. D. Holden. *American Journal of Surgery* [*Amer. J. Surg.*] **102**, 19–28, July, 1961. 6 figs., 18 refs.

The authors have analysed, at the University Hospitals of Cleveland, Ohio, the records of 517 adults diagnosed in the period 1943–57 as having had pulmonary embolism. As the total number of admissions during this time was 287,370 the incidence of pulmonary embolism was thus 0·18%; it was noted that pulmonary embolism occurred in 0·49% of all medical admissions and only 0·094% of surgical admissions. Of the 517 patients, 212 (41%) died; the mortality rose with increasing age, death following in 20% of those aged 30 and in 50% of those aged 70, the over-all mortality, as stated, being 41%. At necropsy, carried out on 159 of the patients, a source of emboli was discovered in the heart in 57%, the deep leg veins in 48%, the thigh, pelvic veins, and inferior vena cava in 41%, the superficial leg veins in 4%, an arm vein in 3%, and the pulmonary artery in 5%. In many patients several possible sources were found.

Clinically, the first symptom of embolism was respiratory distress of some kind in 356 patients (70%). Only 110 patients (20%) had previous symptoms of peripheral venous thrombosis, while 51 patients (10%), all with heart failure, showed no symptoms recognized as due to pulmonary embolism, the diagnosis first being made at necropsy. Many patients had associated diseases, of which heart disease was the commonest, being found in 335 (65%); in those with heart failure the death rate was high (65%). Inflammatory states, which included such conditions as collagen diseases and thrombo-angiitis, were present in 160 patients (31%), with a mortality of 47%. In the 156 patients (30%) who were recovering from an operation pulmonary embolism usually occurred between the 5th and 9th postoperative days and the death rate was 27%. Cancer was present in 51 patients (10%), but 45 of these had other abnormal conditions such as heart disease or inflammation. In only 6 (1%) was cancer the sole associated disease and the authors suggest that the importance of cancer as a cause of pulmonary embolism has been exaggerated; in this group the mortality was 49%. A study of the time of death after pulmonary embolism showed that 80 of the 159 patients who came to necropsy died within 24 hours and that 60 died within less than one hour of the embolism. In 60 patients (38%) death was due to a large embolus, in 81 (51%) to multiple small emboli, and in 18 (11%) to some other cause, the pulmonary embolism being incidental.

An attempt was made to assess the value of treatment with anticoagulant drugs and ligation of veins. No conclusions could be reached about the latter procedure, since it was performed on only 17 patients, of whom 12 also received anticoagulants. Administration of anticoagulants was usually started in patients with signs of peripheral venous thrombosis or pulmonary embolism, the regimen being heparin for 48 hours followed by dicoumarol for about 3 weeks, both in the usual dosage. The results in 249 patients so treated were compared with a control group treated with rest and bandaging, this group consisting of patients admitted between 1943 and 1946 before anticoagulants were in use, those in whom these drugs were contraindicated, those to whom anticoagulants were not given because of delay in making the diagnosis of pulmonary embolism, and lastly those who received anticoagulants for less than 48 hours and who then suffered another embolism, the total in these various categories amounting to 107 patients. Recurrent embolism occurred in 20% of the treated and 60% of the control patients, while 4·7% of the treated group died, compared with 35·5% of the controls. However, when

patients with heart disease were excluded the mortality was 0·8% in the treated group compared with 18·5% in the controls.

[Most of the observations here reported have been recorded before. However, it is right to emphasize how often pulmonary embolism occurs in medical patients, particularly those with heart failure, and how infrequently peripheral venous thrombosis gives a warning. The value of anticoagulant treatment seems certain. Pulmonary embolectomy can be practicable and helpful in only a very small number of patients and these are often very difficult to recognize.] *Arthur Willcox*

1469. **Chronic Bronchitis: a Further Study of Simple Diagnostic Methods in a Working Population**

C. M. FLETCHER and C. M. TINKER. *British Medical Journal* [*Brit. med. J.*] **1**, 1491–1498, May 27, 1961. 4 figs., 15 refs.

A survey of respiratory symptoms, using a self-administered and an interview questionary, morning sputum volume, and ventilatory capacity estimated by the Wright peak expiratory flow meter, was carried out on a random sample of 513 men aged 30 to 59 at the London Transport Executive workshops. Agreement between the answers on cough, phlegm, dyspnoea, and smoking habits in the two questionaries was good, but the written questionary was not returned or was incompletely filled in by a quarter of the men. The lapse rate was only 7% in a group of Post Office clerks. It appears that a self-administered questionary can provide useful information, especially in a population accustomed to clerical work.

Comparison of the results of the present survey with a previous survey of London postmen revealed a similar prevalence of respiratory symptoms in the two populations, but the London Transport employees had fewer chest illnesses than postmen or random samples of men in other urban areas. Possible explanations for this difference are discussed. The relationship between answers to questions about phlegm production and morning sputum volume was closely similar in the two populations, confirming the validity of these techniques in the diagnosis of simple chronic bronchitis.

In both populations, cough, phlegm production, chest illnesses, and impaired ventilatory capacity were more frequent in smokers than in non-smokers. Chest illnesses and impaired ventilatory capacity were more frequent with increasing sputum volume. Prospective study is needed to reveal the reasons for these important associations.—[Authors' summary.]

1470. **Chronic Bronchitis: Controlled Trial of Isoprenaline and Chymotrypsin by Inhalation**

P. O. LEGGAT, C. VERITY, and D. J. NEWELL. *British Medical Journal* [*Brit. med. J.*] **2**, 88–90, July 8, 1961. 1 fig., 7 refs.

At Walker Gate Hospital, Newcastle upon Tyne, 35 patients aged 30 to 65 who had had chronic winter cough and sputum and had lost time from work on account of bronchitis were admitted to a trial to compare the effects on ventilatory capacity, measured by estimating the forced expiratory volume in the first second ($F.E.V._1$), and on the weight of sputum expectorated of an aerosol of finely divided chymotrypsin with isoprenaline administered as a fine powder or as an aerosol with an inert propellant. The sputum was weighed over a 24-hour period and the $F.E.V._1$ was measured one minute, 3 minutes, 3 hours, and 6 hours after the treatment had been given. There was no difference between the effects of either preparation on ventilatory capacity or sputum weight. There was on the whole a very slight improvement in ventilatory capacity and a slight decrease in sputum weight. Five patients developed allergic reactions to the therapy, which had to be discontinued on this account. The trial therefore showed that treatment with chymotrypsin and isoprenaline produces only a very slight, transient improvement in ventilatory capacity, similar for both forms of administration, and that there is a considerable risk of adverse effects. *C. M. Fletcher*

1471. **Nonobstructive Atelectasis: its Occurrence with Pneumonitis**

B. BURBANK, S. S. CUTLER, and S. SBAR. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **41**, 701–716, June, 1961. 3 figs., 30 refs.

The authors describe a small group of 6 cases in which there was disease initially resembling pneumonia. Intense and persistent chest pain followed, lasting for days and diminishing only slowly. Fever lasted for 2 to 3 weeks and was not affected by antibiotics. No pathogenic organisms were isolated from cultures of sputum or blood. Chest radiographs showed an extensive opacity which in most cases was diagnosed as a pleural effusion. This diagnosis, however, was incorrect, because on later review the elevated diaphragm, crowded intercostal spaces, and slight shift of the mediastinum to the ipsilateral side indicated an atelectatic component. The prognosis was favourable; none of the patients died and in spite of a stormy and protracted course all 6 made a full clinical recovery.

The authors consider that the condition is due to atelectasis without obstruction of the bronchi. They produce evidence to suggest that it is caused by active contraction of the lung tissue and the further effects of surface tension in the alveoli. *G. M. Little*

1472. **Pneumonia in Hospital Practice**

N. C. OSWALD, G. SIMON, and R. A. SHOOTER. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **55**, 109–118, July, 1961. 6 refs.

The records of all patients admitted to St. Bartholomew's Hospital [London] with a diagnosis of pneumonia or its complications during the period 1949–58 have been reviewed. Of the 1,330 patients, 861 were males and 469 females; 303 were children under the age of 15. Some 634 (63%) of the adults and 90 (30%) of the children had a pre-existing disease. Respiratory disorders, particularly chronic bronchitis and emphysema, and cardiovascular diseases were by far the commonest concomitants. There were 109 (8·2%) deaths, 98 in adults and 11 in children. Of the adults, 59% were aged 65 or more and 35% were judged to have been

moribund on admission; of the 25% who were under the age of 65 and were not moribund on admission, uncontrolled pneumonic infection, chronic bronchitis and emphysema, and heart disease, seemed to be the principal causes of death. Of the 11 fatalities in childhood, 6 were attributed to uncontrolled fulminating infections. Bronchitis was diagnosed in 38% of the adults and 52% of the patients who died. Cardiovascular disease existed in 12% of the adults and 22% of the deaths. The pneumococcus was found with equal frequency in the sputum of otherwise healthy adults, chronic bronchitics and children. *H. influenzae* was found twice as often in patients with pre-existing chronic respiratory diseases as in those with previously healthy lungs. Homogeneous radiological consolidation was twice as common as mottling, but mottling became relatively more frequent with advancing years. This trend can be accounted for to a large extent by emphysema, in which the opacities were predominantly mottled. In children, associated diseases and pulmonary complications were less common than in adults, but the mortality was high in infancy. The bacteriology of the sputum and the radiological appearances were similar to those seen in adults who did not have chronic respiratory diseases. [See also Hausmann and Karlish, *Brit. med. J.*, 1956, **2**, 845; *Abstr. Wld Med.*, 1957, **21**, 266.]—[Authors' summary.]

1473. **Pulmonary Fungus Infections Associated with Steroid and Antibiotic Therapy**
H. SIDRANSKY and M. A. PEARL. *Diseases of the Chest* [*Dis. Chest*] **39**, 630–642, June, 1961. 7 figs., 17 refs.

At the Charity Hospital of New Orleans there has recently been a definite increase in the incidence of secondary infection of the lungs due to such fungi as *Aspergillus*, *Mucor*, and *Candida*. These infections, which can lead to considerable lung destruction and death, have occurred in patients suffering from chronic debilitating disorders such as malignant disease, leukaemia, and diabetes. In the authors' view administration of steroids and the broad-spectrum antibiotics has contributed to this increased incidence. Of 20 cases seen over a recent 3-year period, 15 had been treated with both steroids and antibiotics and 4 with antibiotics alone; in only one case had neither steroids nor antibiotics been given. It is of interest that 11 of the 20 patients had extrapulmonary infection as well.

At necropsy bronchopneumonia was diagnosed in most cases, but histological examination of lung tissue revealed the true nature of the lesions. Except in cases of infection due to *Candida*, the grey, nodular lesions were surrounded by haemorrhagic areas. It is pointed out that the ante-mortem diagnosis in these cases is difficult, but fungus infection should be suspected in debilitated patients with pneumonic or bronchopneumonic lesions who do not respond to standard treatment. Positive sputum cultures in these cases do not necessarily indicate " secondary contamination ".

The paper contains detailed histories of several cases and also descriptions of the histological changes in tissue produced by the various fungi. *Paul B. Woolley*

1474. **The Occurrence of Intrathoracic Calcification in Sarcoidosis**
H. L. ISRAEL, M. SONES, R. L. ROY, and G. N. STEIN. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **84**, 1–11, July, 1961. 5 figs., 9 refs.

Radiographic evidence of calcification of intrathoracic lymph nodes or of the pulmonary parenchyma was found in 10·1% of 256 patients with sarcoidosis examined at the Jefferson Hospital, Philadelphia. A similar incidence, however, was observed among patients in whom the diagnosis of sarcoidosis had not been established. It seemed likely that the calcification was as often due to histoplasmosis as to tuberculosis. A skin-testing survey revealed tuberculin anergy in 30·1% and histoplasmin anergy in 8·5% of the sarcoidotic patients, the number of negative reactions being significantly greater in the patients than in the controls. Positive reactions to Battery P.P.D. tuberculin prepared from atypical mycobacteria were obtained in 9% of patients with sarcoidosis and in 25% of a " non-sarcoid " group. All these reactors showed positive Mantoux reactions, so some degree of cross-sensitivity was presumed. The presence of intrathoracic calcification could not be related to birthplace, contact with tuberculosis, or hypercalcaemia. Calcification developed during the period of observation in only 2 patients with sarcoidosis, one of whom had chromogenic acid-fast bacilli in the sputum. Its infrequency as a sequel to sarcoidosis in the U.S.A. argues against mycobacteria or fungi being aetiological agents or secondary invaders, and it is noted that the latter appear to be more common in Britain according to the report by Scadding (*Brit. med. J.*, 1960, **2**, 1617; *Abstr. Wld Med.*, 1961, **29**, 366).
D. Geraint James

1475. **The Association of Lung Cancer and Tuberculosis**
A. H. CAMPBELL. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **10**, 129–136, May, 1961. 24 refs.

An investigation by the Australian Repatriation Department of the medical histories of 6,502 tuberculous ex-servicemen showed that their death rate was higher by one-third than the expected death rate in the general population. A more detailed analysis of the causes of death showed that pulmonary tuberculosis rates were double those of the normal population, and that the rate for lung cancer was nearly treble the expected rate, there being 34 actual deaths from this cause compared with 13 expected deaths. The author associates this increase with various pathological studies which have suggested that lung cancer occasionally arises in scar tissue, including tuberculous scars. While the smoking habits of the patients could have increased the rate of lung cancer by a small fraction, tobacco seemed an inadequate explanation for the very large increase.
J. Robertson Sinton

1476. **Observations Concerning the Blood Volume, Red Cells and Erythropoiesis in Patients with Lung Cancer: a Pre- and Postoperative Study.** [Monograph in English]
K. E. J. KYLLÖNEN. *Annales chirurgiae et gynaecologiae Fenniae* [*Ann. Chir. Gynaec. Fenn.*] **50**, Suppl. 101, 1–120, 1961. Bibliography.

Urogenital System

1477. **The Brain in Uremia: a Patho-anatomical Study of Brains from 104 Patients Dying in Renal Insufficiency, with Reference to the Influence of Complicating Factors, Especially Ischemia of the Brain.** [Monograph, in English]
S. OLSEN. *Acta Psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **36**, 1–128, 1961. 20 figs., bibliography.

1478. **An Investigation of the Haemorrhagic Tendency in Renal Failure**
M. L. N. WILLOUGHBY and S. J. CROUCH. *British Journal of Haematology* [*Brit. J. Haemat.*] **7**, 315–326, July, 1961. 5 figs., 27 refs.

Although a variety of abnormalities of blood coagulation and of haemostatic mechanisms have been previously reported in patients with renal failure, none has been found consistently. The bleeding time, clotting time, prothrombin time, the results of Hess's tourniquet test, and platelet counts are frequently normal in subjects with haemorrhagic symptoms. The present study was undertaken at the Radcliffe Infirmary, Oxford, to define more closely the abnormalities of the clotting and haemostatic systems in renal failure, and in the hope that a series of laboratory tests might be developed which would be capable of detecting the presence of a bleeding tendency with reasonable confidence.

Of the 56 patients with renal failure studied, 26 had haemorrhagic symptoms, and of the latter, the Ivy bleeding time was prolonged in 18. The rate of bleeding from the skin punctures was greater than normal in many of these cases and also in 5 of the 8 subjects whose bleeding times were within the normal range. The prothrombin consumption index (P.C.I.) was the only test of blood coagulation found to be abnormal in a significant number of the haemorrhagic group, and its abnormality was closely related to the defect in cutaneous haemostasis as measured by the Ivy bleeding time. In tests using native platelet-rich and platelet-poor plasma from affected subjects and normal controls it was shown that the abnormal P.C.I. values were due in most cases to a qualitative platelet defect; in 3 cases a circulating inhibitory substance seemed to be responsible. Thromboplastin generation tests were normal in all cases showing an abnormal P.C.I., suggesting that the latter test is a more sensitive index of platelet function. Thrombocytopenia was slightly more common in the haemorrhagic group, but was a factor in the production of haemorrhage in only a small minority of patients. A positive result in the tourniquet test was obtained in only 5 patients, of whom 3 had obvious purpura, and was thus of little value in detecting a bleeding tendency. Only 2 patients, both with acute anuria, showed a prolonged one-stage prothrombin time and whole-blood clotting time.

It is concluded that the most useful laboratory tests in the detection of a bleeding tendency in renal failure are the Ivy bleeding time, measurement of the rate of blood loss from skin punctures, and the P.C.I. determined on whole blood. An acquired thrombopathy is considered to be responsible for these three abnormal measurements in most cases. *A. Brown*

1749. **Acute Glomerulonephritis in Elderly Patients: Report of Seven Cases Over Sixty Years of Age**
A. H. SAMITY, R. A. FIELD, and J. P. MERRILL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **54**, 603–609, April, 1961. 7 refs.

This is a report from the Peter Bent Brigham and Massachussetts General Hospitals and Harvard Medical School, Boston, of 7 cases of acute glomerulonephritis in 4 male and 3 female patients all over the age of 60. The diagnosis was established in 2 cases by renal biopsy and in one of these and in 2 others it was subsequently confirmed at necropsy; in 3 cases the diagnosis was made on clinical grounds. The features of the illness were rather atypical and were perhaps modified by pre-existing changes. The commonest symptoms were dyspnoea and oedema (3 patients having pulmonary oedema). One patient presented with painless haematuria and one with sudden anuria. Three gave a history of a preceding throat infection (but as the diagnosis was not always suspected the others may not have been closely questioned about this). The antistreptolysin titre was estimated and is stated to have been raised in all cases. (In one, however, the titre was only 159 Todd units.) Three of the patients died in hospital, 2 succumbing to severe pulmonary infection. The others recovered fairly satisfactorily. Because of the atypical presentation the diagnosis was considered initially in only one case.

The authors conclude that although commonly a disease of childhood and young adults, acute glomerulonephritis may occur at any age.
C. Bruce Perry

1480. **Post-streptococcal Glomerulonephritis: Histopathologic and Clinical Studies of the Acute, Subsiding Acute and Early Chronic Latent Phases**
R. B. JENNINGS and D. P. EARLE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **40**, 1525–1557, Aug., 1961. 2 figs., bibliography.

1481. **Acute Glomerulonephritis in the Adult. Longitudinal, Clinical, Functional and Morphologic Studies of Rates of Healing and Progression to Chronicity**
D. S. KUSHNER, S. H. ARMSTRONG JR., A. DUBIN, P. S. SZANTO, A. MARKOWITZ, B. P. MADUROS, J. M. LEVINE, G. L. RIVER, T. N. GYNN, and J. P. PENDRAS. *Medicine* [*Medicine (Baltimore)*] **40**, 203–240, May, 1961. 9 figs., bibliography.

Endocrinology

1482. **Gastric Acid Secretion and Mucosal Appearances in Addison's Disease and Hypopituitarism**
A. W. M. SMITH, I. W. DELAMORE, and A. W. WILLIAMS. *Gut* [*Gut*] **2**, 163–167, June, 1961. 24 refs.

That gastric acid secretion is depressed in Addison's disease has been known for many years. The authors of this paper from the Royal Infirmary, Edinburgh, have made a systematic investigation into the quantitative changes in gastric acid secretion and the gastric mucosal appearances in 14 patients with Addison's disease and 10 with hypopituitarism. The average age of the patients with Addison's disease was 43 years, and of those with hypopituitarism 52 years. Gastric secretion was estimated by the modified histamine secretion test, the gastric juice being collected by continuous suction for an hour after histamine stimulation. Statistical analysis of the acid secretory response showed a clear-cut depression both in patients with Addison's disease and those with hypopituitarism as compared with healthy subjects. The results (in mEq.) are given below.

	Males		Females	
	Mean	S.D.	Mean	S.D.
Addison's disease ..	5·90	±3·24	3·30	±1·65
Hypopituitarism ..	—	—	5·98	±1·52
Healthy subjects ..	24·11	±1·53	17·20	±1·36

Thus the study confirms previous observations of diminished gastric secretion of hydrochloric acid in these two diseases.

Examination of biopsy specimens of the gastric mucosa from 12 patients with Addison's disease and 9 patients with hypopituitarism revealed abnormal histological appearances in 8 of the former and 3 of the latter.

It is concluded that the greater frequency of functional and structural changes in Addison's disease than in hypopituitarism may be a reflection of the greater depression of adrenal function in the former condition.

I. McLean Baird

THYROID GLAND

1483. **Sporadic Goitre and Cretinism Due to the Production of an Abnormal Thyroid Protein**
J. H. HUTCHISON. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **54**, 533–537, July, 1961. 4 figs., 16 refs.

The author describes from Glasgow Royal Infirmary the results of studies on 6 cases of goitre, all similar in type and all outside the four accepted types of goitre due to enzyme deficiencies. Three of the patients were sisters with enormous goitres, one being hypothyroid, 2 were cretinous brothers with small goitres, and the 6th was a mildly hypothyroid boy with a moderate goitre. At 48 hours after a tracer dose of radioactive iodine (^{131}I) all showed a high serum ^{131}I level within the thyrotoxic range, but only a small proportion of the protein-bound ^{131}I was extractable by butanol (which extracts thyroxine and iodotyrosines). Thus there appeared to be some abnormal iodinated compound present in the protein-bound iodide in the serum.

In one case chromatographic and electrophoretic studies on extracts of thyroid tissue, removed at thyroidectomy 48 hours after a dose of 1 mc. of ^{131}I, revealed that there was no stainable thyroglobulin present, but that there was on the other hand an abnormal iodinated thyroprotein closely similar to, if not identical with, the abnormal substance found in the serum. The author suggests that this abnormal thyroprotein is liberated into the blood, but does not release thyroxine in the tissues. The development of goitre is presumably due to compensatory overactivity of pituitary thyrotrophin, the adequacy of this compensatory effort determining whether the patient remains euthyroid or not. The familial incidence indicates that this type of goitre is a genetically determined inborn error of metabolism.

A. Gordon Beckett

1484. **Thyroglobulin Antibodies in 1,297 Patients without Thyroid Disease**
O. W. HILL. *British Medical Journal* [*Brit. med. J.*] 1, 1793–1796, June 24, 1961. 3 figs., 9 refs.

It is known that the serum of patients suffering from thyroid disorders, particularly Hashimoto's disease, often shows antibodies to thyroglobulin. In a series of 1,297 sera tested at the Middlesex Hospital, London, by the tanned erythrocyte haemagglutination technique (of which 17 were excluded as coming from patients with thyroid disease) positive results at a dilution of 1 in 25 were found to be six times more frequent in women than in men. At ages 40 to 69, 10% of all women in this series had circulating thyroid antibodies to a titre of over 1:25. This finding is important in view of the significance attached to the finding of such antibodies in women with thyroid disease.

G. S. Crockett

1485. **Blood Radiation Dose after ^{131}I Therapy of Thyrotoxicosis: Calculations with Reference to Leukaemia**
M. GREEN, M. FISHER, H. MILLER, and G. M. WILSON. *British Medical Journal* [*Brit. med. J.*] **2**, 210–215, July 22, 1961. 8 figs., 37 refs.

From the University of Sheffield and the Sheffield National Centre for Radiotherapy the authors report estimates of the blood radiation dose received by 191 patients with thyrotoxicosis treated by radioactive iodine (^{131}I). Blood samples were taken from each patient 1, 2, 5, 9, 14, and 28 days after treatment with a single dose of ^{131}I. Calculations of the blood radiation dose were then made, taking into account (*a*) the first phase, when radioactivity is circulating as iodide, (*b*) the

second (thyroxine) phase, when radioactivity is mainly protein-bound, and (*c*) radiation from ^{131}I in the thyroid gland.

The mean dose was found to be $1{\cdot}7 \pm 0{\cdot}06$ rads per mc. given. It is shown that the radiation dose to the blood is related to the amount of ^{131}I administered and, more closely, to the protein-bound ^{131}I level measured 48 hours after a preliminary tracer test. A nomogram is provided that can be used for calculating the blood radiation dose from these data. The relationship between blood dose and bone-marrow dose is discussed and the consequent risk of leukaemia estimated. The mean total blood radiation per patient in a series of 802 patients was 17 rads. It is therefore suggested that the risk of leukaemogenesis in ^{131}I therapy is slight.

[This paper should be studied in full as it is an extremely valuable quantitative help in assessing the possible hazards of ^{131}I compared with other methods of treatment of thyrotoxicosis.] *K. E. Halnan*

1486. **Chronic Thyrotoxic Myopathy**

A. G. W. Whitfield and W. A. Hudson. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **30**, 257–267, July, 1961. 6 figs., 33 refs.

The clinical study of chronic thyrotoxic myopathy here reported from the Queen Elizabeth Hospital, Birmingham, is based on 5 cases of the disorder observed by the authors and some 60 cases reported in the literature since this rare condition was first noted in 1895. Although 4 of the authors' 5 patients were women, 60% of previously recorded cases have been in males. In view of the fact that thyrotoxicosis is much more common in females than in males, it would seem that men are especially prone to this myopathy. In nearly all the previously reported cases, and in all of the authors', symptoms of thyrotoxicosis had been present for less than a year, the muscular weakness showing itself some weeks or months after the onset. Patients with long-standing thyrotoxicosis are unlikely to develop myopathy. Most patients who have developed the disorder have been severely thyrotoxic, with a greatly increased basal metabolic rate and a high uptake of radioactive iodine.

The distribution of the muscular weakness is strikingly constant, affecting the shoulder and pelvic girdles, the quadriceps and upper arms, and the small muscles of the hands. In no recorded case has there been alteration in the reflexes or any sensory loss, but muscle fibrillation did occur in one of the present cases which was complicated by diabetes. In none of the authors' cases did the injection of neostigmine produce any increase in power; in some reported cases such improvement has been described, but it seems probable that this was due to the coincident presence of myasthenia gravis. Muscle biopsy, carried out on 4 patients, showed atrophy of muscle fibres and their replacement by fat, proliferation of subsarcolemmal nuclei, and infiltration between muscle fibres of lymphocytes and histiocytes. Similar changes may be observed in other muscle disorders. With successful treatment of the thyrotoxicosis, whether surgical or medical, muscle weakness and wasting disappeared within a few months of the return of normal thyroid function. Full case reports are presented, together with photomicrographs of muscle biopsy specimens.

[This paper contains a valuable list of references.] *Kenneth Stone*

ADRENAL GLANDS

1487. **Functional Relationship between Adrenal Medullary and Cortical Hormones in Man**

E. J. Ross. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **30**, 285–296, July, 1961. 2 figs., 18 refs.

Various previous studies have seemed to imply that a functional relationship between the cortex and medulla of the adrenal gland—tissues which are embryologically dissimilar—may exist in man, and suspicion of such a relationship was confirmed by observations on a female patient aged 63 referred to University College Hospital, London, with a phaeochromocytoma which showed that when adrenocortical insufficiency developed the blood pressure fell, but the urinary output of catechol amines remained high. This finding suggested that there was a relationship between the pressor activity of catechol amines and the adrenocorticoids or the metabolic effects of the latter.

Experiments were therefore performed on normal subjects and on patients with adrenal insufficiency in an endeavour to determine the nature of the relationship. The changes in blood pressure produced by infusions of noradrenaline at a rate of 0·1 and 0·2 μg. per kg. body weight per minute in a bilaterally adrenalectomized patient with an adrenal crisis were not significantly different whether they were given together with an infusion of 100 mg. of hydrocortisone in normal saline or not. In a patient with Addison's disease similar infusions of noradrenaline were given before and after treatment with 50 mg. of cortisone and 6 g. of sodium chloride daily for 15 days; the pressor response to the lower dose of noradrenaline was greatly increased after treatment. Again, the pressor responses to infused noradrenaline in a patient with hypopituitarism were considerably greater than those in normal individuals. The secretion of hydrocortisone in the patient with hypopituitarism was estimated to be about 10% of normal, but aldosterone secretion might be expected to be in the region of 60% of normal. Thus the enhanced activity of the noradrenaline might have been due to the aldosterone or to a secondary effect of it. In order to differentiate between these two alternatives a normal subject was given a rice diet for 14 days in which the sodium intake was 3 mEq. per day. By the end of this period his urinary excretion of aldosterone showed a fourfold increase. Despite this rise in excretion (and presumably in secretion) of aldosterone his sensitivity to a noradrenaline infusion was reduced. Another normal subject was given spironolactone (1,000 mg. daily) for 5 days to antagonize aldosterone, this being followed by a low-sodium diet for 14 days. At the end of this time his sensitivity to noradrenaline was decreased, and restoration of plasma volume to normal with dextran did not affect it. However, the infusion of one litre of normal saline did increase the sensitivity to some extent. In 4

normal subjects it was shown that the rise in diastolic blood pressure produced by an infusion of noradrenaline was related to the fall in plasma sodium concentration which was also produced by the infusion. It is concluded that the modification of the pressor activity of noradrenaline by adrenal cortical hormones is due to modification of the intracellular sodium concentration in the smooth muscle of the arteriolar wall. These studies thus confirmed that there is a functional relationship between the hormones secreted by the two parts of the adrenal gland, but that it is indirect. *P. A. Nasmyth*

1488. **Accessory Adrenocortical Function after Adrenalectomy in Patients with Breast Cancer**
A. W. Sim, R. Hobkirk, D. W. Blair, H. J. Stewart, and A. P. M. Forrest. *Lancet* [*Lancet*] **2**, 73–76, July 8, 1961. 5 figs., 21 refs.

At the Western Infirmary, Glasgow, 6 patients who had undergone bilateral adrenalectomy and oophorectomy for metastatic carcinoma of the breast which had relapsed after initial regression were investigated to determine whether there was any evidence of returned adrenal function. The investigations comprised serial estimations of the excretion of total 17-ketosteroids and other steroids in the urine and estimation of the plasma hydroxycorticosteroid level before, during, and after withdrawal of cortisone maintenance therapy for a variable period. During this period there was a gradual fall in blood pressure, in steroid output in the urine, and in the plasma hydroxycorticosteroid level. The fall was not reversible by the intravenous administration of corticotrophin.

The authors conclude that the relapse of metastatic mammary carcinoma after an initial response to adrenalectomy and oophorectomy results from the ability of the cancer cell to resume active growth in the absence of hormonal factors and is not due to the development of functioning accessory adrenocortical tissue.

I. McLean Baird

DIABETES MELLITUS

1489. **Perinatal Mortality in Diabetic Pregnancy: the Relationship to Management during Pregnancy and to Foetal Age and Weight.** [In English]
E. Brandstrup, M. Osler, and J. Pedersen. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **37**, 434–440, July, 1961. 4 refs.

On the basis of their experience at Rigshospitalet, Copenhagen, the authors discuss certain factors bearing on the perinatal mortality in a large series of infants born to diabetic mothers, using the term perinatal mortality to include stillbirths and neonatal death (that is, within 10 days) of infants weighing 1,000 g. or more at birth. Of the 643 babies studied, 157 were born in the period 1926–45 and 486 from 1946 to 1960; though the treatment of diabetes differed in these two periods, only the duration of the mothers' treatment before delivery and the infants' birth weight and foetal age are considered, the former being divided into two periods: long-term treatment, that is, attendance by the mother at the authors' clinic 53 days or more before delivery, and a "short-term" group, which included mothers in pre-coma when first seen and those whose baby died or was delivered within 8 days of the mother's first attendance. The average stay in hospital before delivery was 45 days for the long-term group and 15 days for the short-term group.

In the period 1946–60 perinatal mortality decreased as the duration of treatment increased, the foetal loss in the short-term group being 29% compared with 18% in the long-term group and with only 12% of the 111 cases in which treatment extended to 70 days or more. In the period 1926–45 the comparable mortality was 38%. Throughout the whole period 1926–60, of 106 babies born within the foetal age 252–266 days and birth weight 3,500 to 3,950 g., only one died. This age and weight are considered to be particularly favourable for the infant, and the authors discuss various maternal factors which may help to produce a baby of such a suitable gestational age and birth weight. Investigation of maternal age, weight, height, parity, weight gain, diabetic complications, and toxaemia showed no significant features.

F. P. Hudson

1490. **Prednisone–Glycosuria Test for Prediabetes**
G. F. Joplin, R. Fraser, and K. J. Keeley. *Lancet* [*Lancet*] **2**, 67–71, July 8, 1961. 4 figs., 30 refs.

In this study reported from the Postgraduate Medical School of London the authors use the term prediabetes to mean that state in apparently healthy subjects with no clinical evidence of diabetes and whose blood and urinary sugar levels are still normal who nevertheless later show an increased liability to develop diabetes. Many of the patients in this group are mothers who have had otherwise unexplained stillbirths or abnormally large babies. One method hitherto used to detect such patients has been the performance of a standard glucose tolerance test after the ingestion of glucose preceded by oral cortisone, 2 doses each of 50 mg. given at 8½ and 2 hours before the test.

The result of this test, however, is influenced by the rate of glucose absorption. This disadvantage the present authors now show can be overcome by simply assessing the hyperglycaemic and glycosuric response to a corticosteroid without giving any extra oral glucose, thus by-passing the problem of differing absorption rates. After 3 days of controlled diet and a simple glucose tolerance test (which excludes frank diabetics) the rate of urinary excretion of glucose during an 11-hour overnight fast is determined following the oral administration of 3 doses each of 20 mg. of prednisone at midday, 4 p.m., and 8 p.m., urine being collected from 10 p.m. to 6 a.m. In 18 normal subjects and 11 pregnant but otherwise normal women, the rate of urinary glucose excretion never exceeded 60 mg. per hour. In 25 out of 47 suspected cases of prediabetes, including 10 of 21 relatives of known diabetics, this rate was over 60 mg. per hour. Those subjects with abnormally high rates showed a higher mean blood sugar level at midnight during the test than did those with normal urinary findings; this observation, it is suggested, will probably provide a means of distinguishing false positive results

due to the presence of a lowered renal threshold. However, some patients with renal glycosuria may also be prediabetics. Various aspects of the problem of prediabetes and the possible value of the new test are discussed. *H.-J. B. Galbraith*

1491. **Prediabetes in Mothers of Large Infants**
D. A. Davey, G. F. Joplin, and R. Santander. *Lancet* [*Lancet*] **2**, 71–73, July 8, 1961. 2 figs., 19 refs.

Many women who give birth to abnormally large infants develop diabetes, usually after an interval of years. In some of these women the result of a glucose tolerance test is abnormal during pregnancy, but reverts to normal in the puerperium. A more sensitive test for the detection of these prediabetic subjects has been described by Joplin *et al.* [see Abstract 1490] and in this paper from Hammersmith Hospital, London, the present authors report preliminary observations on the application of this prednisone–glycosuria test.

The urinary glucose excretion rates after prednisone in 11 normal pregnant women did not differ significantly from those in 10 normal men and non-pregnant women. The combined mean excretion rate for these two groups was $31{\cdot}8 \pm 11{\cdot}9$ mg. per hour. The statistical probability of the proposed upper normal level (60 mg. per hour) being exceeded by chance is calculated to be less than 1 in 100.

On 13 mothers of large infants 16 prednisone–glycosuria tests were then performed either during the year after delivery or during the early months of a subsequent pregnancy; they revealed that 9 of these 13 patients showed an abnormally high glucose excretion rate. The subsequent obstetric and medical history of such patients must now be followed to determine finally whether this test is a valid one for prediabetes. Such a diagnosis is of more than academic importance because there is evidence that the treatment of prediabetic pregnant women by carbohydrate restriction, with or without insulin, reduces the perinatal foetal mortality.
H.-J. B. Galbraith

1492. **Lipoprotein Elevations of Diabetics on Tolbutamide as Compared to Lipoprotein Levels during Insulin Therapy: Preliminary Observations**
S. R. Greenberg, R. G. Klotz, and J. T. Beardwood Jr. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **241**, 718–726, June, 1961. 2 figs., 25 refs.

Working at the Abington Memorial Hospital (associated with the University of Pennsylvania), the authors have studied the serum lipoprotein pattern in 13 patients with diabetes of maturity onset before and after their transfer from insulin to tolbutamide therapy; the disease had been well controlled with doses of 15 to 40 units of insulin daily.

One month after the change to tolbutamide 11 of the 13 patients showed a rise in the lipoprotein fraction bound to β globulin (the β lipoprotein), the mean value rising by 9%. After 6 months the mean rise had increased to 21%. There was no difference in the blood sugar or serum cholesterol levels during the study. Since these preliminary observations suggest that tolbutamide may not be so effective as insulin in preventing the long-term vascular complications of diabetes the authors are planning a more extensive study of the effect of tolbutamide on the blood lipid levels.
A. Gordon Beckett

1493. **Experiences with Phenformin: a Two-year Study**
R. S. Walker and R. Hannah. *Diabetes* [*Diabetes*] **10**, 275–279, July–Aug., 1961. 1 fig., 9 refs.

The place of diguanides in the treatment of diabetes is not so well established as that of the sulphonylurea compounds. This report from Law Hospital, Carluke, Lanarkshire, presents the experience gained over 2 years in the treatment of 117 diabetic patients with phenformin (N′-phenethyldiguanide). Of these patients, 37 were new cases not controlled by diet alone, 16 were patients in whom it had been impossible to achieve or maintain control with sulphonylurea drugs, and 64 were patients poorly controlled by insulin. None were obese. During treatment carbohydrate intake was limited to 170 g. per day or less, and phenformin was given in tablet form twice daily after meals, beginning with 50 mg. per day and increasing to the required dose, the final mean dose being 116 mg. per day. Doses in excess of 150 mg. per day did not usually enhance the hypoglycaemic effect.

In the assessment 20 patients (17%) were classified as early failures, in 14 cases because of lack of hypoglycaemic action and in 6 because of toxic effects. A further 36 (31%) were judged to be late failures, since 12 of them showed secondary failure of hypoglycaemic action, 11 developed keto-acidosis, and 13 had troublesome alimentary symptoms. In 61 (52%), however, the result was reckoned as a success, albeit partial in 19 cases in that although insulin could be reduced in dosage by one-third as a result of the administration of phenformin, it could not be stopped entirely; in the remaining 42 success was complete in that control was achieved with diet and the diguanide alone. Phenformin was of most value in the 56 patients with "adult, stable" diabetes, 35 (63%) of whom were completely controlled. In the "juvenile, unstable" group there were no complete successes, although 10 out of 37 (27%) were helped by the drug. Phenformin was of some value in 25 (68%) of 37 patients who had received no previous treatment, but in only 40% (25 out of 64) of those previously treated with insulin. Phenformin successfully controlled 22 out of 26 (85%) cases of adult, stable diabetics previously untreated.

Although the hypoglycaemic action of the drug is impressive, the antiketotic action is slight or absent, and ketosis is a real danger. It occurred in 34 cases (29%) in this series, 17 of which were of the juvenile, unstable type. The development of the ketosis is sudden and unpredictable and cannot be related to blood sugar levels. In 11 cases (9%) it led to withdrawal of phenformin, and in one case appeared to be responsible for the patient's death. Nausea or diarrhoea occurred in 41 patients (35%) and caused abandonment of phenformin therapy in 18 cases.

[This is a very valuable report on the uses and limitations of this diguanide drug.] *T. B. Begg*

The Rheumatic Diseases

1494. **Sinus Arrhythmia in Rheumatic Fever**
M. C. JOSEPH and L. TENCKHOFF. *American Heart Journal* [*Amer. Heart J.*] **61**, 634–639, May, 1961. 23 refs.

A study was carried out at the House of the Good Samaritan, Boston, Massachusetts, in an attempt to determine the relationship between sinus arrhythmia and acute rheumatism and rheumatic heart disease. Two groups of children were studied—85 in an initial attack of rheumatic fever and 50 with a recurrence of rheumatic fever. The first group was subdivided according to whether carditis was or was not present. A group of 93 children who had not had rheumatic fever and whose hearts were clinically normal served as a control. The degree of sinus arrhythmia was determined by studying the standard electrocardiograms and measuring the maximum and minimum R–R intervals together with the average of 6 R–R intervals. The frequency index was calculated by subtracting the shortest from the longest R–R interval and dividing the result by the mean multiplied by 100.

In the first group the frequency index in patients with normal hearts was the same as that in the controls, but in those with carditis it was lower. However, these latter had a higher average heart rate. When patients with rates below 100 per minute were studied separately there was no difference between the controls, patients with normal hearts, and those with carditis. On the other hand, in patients with heart rates over 100 the frequency index was the same in those with rheumatic fever whether carditis was present or not; in both groups, however, it was much lower than in the controls with similar heart rates. On discharge, both groups showed a similar degree of sinus arrhythmia.

The 50 children with a recurrence of rheumatic fever were older than those with a first attack. The frequency of sinus arrhythmia was much lower in patients with a recurrence than in those with carditis in a first attack. Similarly, even at heart rates over 100, the incidence was lower in those with a recurrence than in any other group. It is suggested that the decrease in the incidence of sinus arrhythmia is due to involvement of the sino-auricular node and that the low incidence in the group with a recurrent attack may be due to permanent damage to the node. *C. Bruce Perry*

1495. **Further Investigations into the Treatment of Acute Gout with Steroids.** (Nuevas investigaciones sobre el tratamiento del ataque de gota con esteroides)
A. R. MORENO. *Archivos argentinos de reumatologia* [*Arch. argent. Reum.*] **25**, 5–7, Jan.–Apr. [received July], 1961.

At the Antirheumatism Centre, Buenos Aires, the author has treated attacks of gout with corticosteroids. In 16 attacks he gave 8 mg. of dexamethasone-21-phosphate intravenously, followed (in 7 cases) by 0·75 mg. of the same drug orally every half hour. In 9 of the attacks the pain rapidly disappeared, while in the remainder it did so within 2 hours. In another 28 attacks he gave 5 mg. of prednisolone (or its equivalent in other corticosteroids) every 15 minutes for one hour and thereafter half-hourly. In 9 attacks the pain had gone in 2 hours, in 14 in 3 hours, and in the remaining 5 in 4 hours. *Allan St. J. Dixon*

CHRONIC RHEUMATISM

1496. **The Local Treatment of Morton's Metatarsalgia with Steroids.** (Metatarsalgia de Morton, tratamiento local con esteroides)
A. C. CARUSO. *Archivos argentinos de reumatologia* [*Arch. argent. Reum.*] **24**, 8–10, Jan.–Apr. [received July], 1961.

The author, writing from the Antirheumatism Centre of the Faculty of Medical Sciences, Buenos Aires, briefly reviews Morton's own description (1876), as well as that of later authors, of Morton's metatarsalgia and concludes that there is probably more than one cause for this disorder. In his own 9 cases tenderness was found between the regions of the epiphyses of the 4th and 5th metatarsal bones, occasionally between the 3rd and 4th or 2nd and 3rd, and in some cases also between the shafts of the bones. The pain could be very severe, disturbing sleep, and was noted especially on removing the shoe. It was experienced locally in most cases, but in a few was referred to the corresponding toes. Treatment by the local injection of "0·75 to 1·0 c.c." of prednisolone tertiary-butyl-acetate and a local anaesthetic often gave striking and immediate relief. Of 7 patients so treated, 4 obtained lasting cure (after up to five injections); in these cases the pain was probably due to local inflammatory and vascular changes. The 3 patients who did not respond were thought to have interdigital neuromata. *Allan St. J. Dixon*

1497. **Adrenal Suppression Due to Intra-articular Corticosteroid Therapy**
S. SHUSTER and I. A. WILLIAMS. *Lancet* [*Lancet*] **2**, 171–172, July 22, 1961. 4 figs., 13 refs.

Because of reports of systemic effects resulting from the use of corticosteroids given intra-articularly the present study was undertaken at Cardiff Royal Infirmary to determine whether sufficient steroid was in fact absorbed following intra-articular injection to suppress activity of the adrenal glands, and if so at what dosage this would occur. The study was carried out on 12 patients (4 male and 8 female) between the ages of 56 and 74, of whom 6 had active synovitis of the knee-joint from rheumatoid arthritis, 6 were suffering from osteoarthritis, and none had previously received steroid therapy. In order to minimize the effect of the diurnal variation in

plasma cortisol concentration, all blood samples were taken between 9 and 10 a.m. After one or two control samples had been taken, triamcinolone diacetate in a dosage varying from 25 to 100 mg. was injected into the affected joint and further blood samples taken daily for 4 to 6 days. Triamcinolone was chosen as it does not react significantly with the Porter–Silber reagent used in the determination of plasma cortisol concentration.

In 4 out of the 5 patients receiving a dosage of 75 mg. or more of triamcinolone daily the plasma cortisol concentration fell below the lower limit of normal, with complete suppression adrenal function, this latter recovering in the course of the subsequent 4 or 5 days. Of the 3 patients given 50 mg. of triamcinolone daily, 2 showed a fall in the plasma cortisol concentration, which rose again in 3 or 4 days, while in the 3rd case there was complete adrenal suppression over this period. Although in 3 out of the 4 patients receiving 25 mg. daily a fall in plasma cortisol levels occurred, this was less impressive than with larger doses and was very transient. On the basis of these results the authors suggest that adrenal suppression is regularly produced by daily intra-articular doses of triamcinolone of 75 mg. or more and may well occur with smaller doses. It is suggested that the relatively lengthy adrenal suppression after a single intra-articular injection is indicative of continued absorption of this steroid. The danger of adrenal atrophy resulting from repeated intra-articular injection of steroids is pointed out. *B. M. Ansell*

1498. **Specificity of the Reaction between Rheumatoid Factors and Gamma Globulin**

H. H. FUDENBERG and H. G. KUNKEL. *Journal of Experimental Medicine* [*J. exp. Med.*] **114**, 257–278, Aug. 1, 1961. 2 figs., bibliography.

This paper from the Rockefeller Institute, New York, gives a detailed report of investigations on the reactions of the rheumatoid macroglobulin (rheumatoid factor), based on the concept that it may represent a form of antibody γ globulin. It has previously been shown by various authors that certain rheumatoid sera can be employed to detect genetic differences between human γ globulins. In the present investigation a modification of the test system of Waller and Vaughan gave results indicating a high degree of specificity for the reaction between individual rheumatoid factors and γ globulins representing different incomplete anti-Rh_0 antibodies. Eight factors of differing specificity, although "undoubtedly several more exist", were distinguished in rheumatoid sera according to their reactivity with the specific individual γ globulins. In many instances the reaction of rheumatoid factor with its own γ globulin was poor. Many different agglutination patterns were demonstrable and some could be correlated with the presence or absence of the known genetically determined (Gm)γ-globulin groups. Differential absorption showed that some rheumatoid sera had multiple specificities. Attempts to inhibit the sensitized sheep cell reaction were uniformly unsuccessful under conditions where clear inhibition would be obtained in the Rh system. Sera selected from various non-rheumatoid diseases which tend to give positive agglutination reactions in the sheep cell tests with human γ globulin as the reactant showed a limited range of specificity with the anti-Rh_0-coated cells. The 7S γ globulin from sera with only one specificity in their rheumatoid factor was separated by density gradient ultracentrifugation and typed for its genetic group in a standard Gm-typing system. It was found to lack the specific antigen, but contained instead the genetic allele. Reactivity of γ globulin with rheumatoid factor to produce the 22S complex appeared to be a universal property of different γ globulins unrelated to specificity in the Rh system. No selectivity comparable to that in the Rh systems could be demonstrated in precipitin reactions with soluble γ-globulin aggregates.

The finding that certain rheumatoid factors failed to react with their own γ globulin in the highly specific incomplete Rh_0 system while reacting well with sera of persons of different genetic types raises the possibility that these proteins actually are isoantibodies analogous to isohaemagglutinins. "Evidence to support the antibody concept of 'rheumatoid factor' has been accumulated during the past few years, but evidence of such marked specificity has not hitherto been brought forward." *Harry Coke*

1499. **Serological Investigations with the Ultracentrifuge, Electrophoresis, and the So-called Rapid Latex Test in Rheumatoid Arthritis.** (Serumuntersuchungen mit der Ultrazentrifuge, der Elektrophorese und dem sog. Latex-Schnelltest bei der primär-chronischen Polyarthritis)

D. KOCH and H. ODENTHAL. *Deutsches Archiv für klinische Medizin* [*Dtsch. Arch. klin. Med.*] **207**, 109–117, 1961. 1 fig., 23 refs.

The sera of 37 patients with rheumatoid arthritis were subjected at the Medical Academy, Düsseldorf, to the latex fixation slide test, electrophoresis of the serum proteins, and examined for the sedimentation pattern after ultracentrifugation which was performed at 48,000 *g* for 120 minutes, the resulting gradient being measured planimetrically. The most striking abnormality was an increase in the macroglobulins, which also showed an abnormally high sedimentation coefficient. In 17 of the sera a second macroglobulin component was seen. There was no correlation between the sedimentation pattern on ultracentrifugation and the results of the other two tests. *G. W. Csonka*

1500. **An Evaluation of a Polystyrene–Globulin Particle Flocculation Test for Serum Rheumatoid Factor**

J. G. MAYNE and D. R. MATHIESON. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **36**, 365–371, July 19, 1961. 13 refs.

Serum samples from 608 patients with various musculoskeletal diseases and 26 whose serum reacted with syphilis antigen were studied for rheumatoid factor with use of a polystyrene–globulin reagent, RA-test (Hyland). Results were positive in 56% of the cases of definite rheumatoid arthritis, 16% of suspected rheumatoid arthritis, and about 5% of the group of patients with rheumatoid variants (juvenile rheumatoid arthritis, rheumatoid spon-

dylitis, Reiter's syndrome, psoriatic arthritis, rheumatoid arthritis associated with psoriasis, arthritis associated with chronic ulcerative colitis, or regional enteritis), rheumatic diseases other than rheumatoid arthritis or variants, and seropositive lues. Weakly positive results were found in an additional 10 and 5% of patients with definite and suspected rheumatoid arthritis, respectively, and in 3 to 8% of patients classed in the other groups. Negative results were found in 35% of patients with definite rheumatoid arthritis, 79% of patients with suspected rheumatoid arthritis, and in 89 to 92% of patients classed in other groups.

The test is easy to perform. The end point is distinct and simple to read. The reagent is stable, reproducible, and readily available. The test is useful as an aid in the diagnosis of rheumatoid arthritis. A negative finding does not exclude the diagnosis of rheumatoid arthritis, but a positive finding is added objective support for the diagnosis.—[Authors' summary.]

1501. **Aortic Insufficiency in Ankylosing Spondylitis.** (Aorta-insufficiëntie bij spondylitis ankylopoetica)
A. CATS and J. GOSLINGS. *Nederlands tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **105**, 1242–1247, June 24, 1961. 27 refs.

The authors report from the Leiden Rheumatological Clinic, Netherlands, 6 cases of isolated aortic insufficiency associated with ankylosing spondylitis occurring in 5 patients aged 44 to 58 years and one aged 26. No evidence of syphilis or rheumatic fever was found in any of these patients, and Rose's test was negative in all, even when peripheral joint destruction was present; 2 of the patients had suffered from gonorrhoea. In a review of the literature the authors found that aortic insufficiency alone occurred more frequently in ankylosing spondylitis than would be expected by chance. The proportion, about 4% in a group of 500 quoted, increased with the age of the patient, the duration of the disease (10% in cases of 30 years' duration), and with the degree of involvement of peripheral joints (18% after 30 years). In 5 of the 6 patients described the spondylitis had been present for 15 years or more. Evidence for a specific type of pathological lesion and for disordered cardiac conduction as evidenced by an increased P–R interval is also quoted. It is pointed out that the recognition of the syndrome of aortic insufficiency in association with spondylitis will avoid unnecessary prolonged prophylaxis against rheumatic fever. *B. Golberg*

1502. **The Spirogram in Ankylosing Spondylitis: the "Reversed Emphysema" Sign**
B. H. BASS and W. G. WENLEY. *Annals of Physical Medicine* [*Ann. phys. Med.*] **6**, 105–108, Aug., 1961. 4 figs., 6 refs.

This paper from the London Hospital discusses the use of a low-resistance spirometer as an aid to the diagnosis of ankylosing spondylitis. The kymograph was set to rotate at 250 mm. per minute and the patient was instructed to take three rapid deep breaths, in and out, through the mouth with the face-piece pressed tightly to the face. The maximum inspiratory flow rate (M.I.F.R.) and maximum expiratory flow rate (M.E.F.R.) were then measured from the slope of the tracing.

In healthy patients steep slopes result and the flow rates are between 400 and 600 litres per minute. In contrast, in emphysema, as a result of expiratory obstruction, the M.E.F.R. is considerably decreased, giving a more shallow slope, but the M.I.F.R. is usually normal. Spirometry was carried out at the same time of day on 20 patients suffering from ankylosing spondylitis of varying degrees of severity and 7 patients suffering from rheumatoid arthritis. The tracings were compared with those from 11 patients with pulmonary emphysema and from a healthy subject. The values for the M.I.F.R. were plotted against those for the M.E.F.R. and the average relationship between the two values in each disease also expressed graphically. The slope of the graph for ankylosing spondylitis was the flattest of the three, that for emphysema being much steeper owing to the relative sparing of the M.I.F.R. The graph for rheumatoid arthritis was intermediate between the other two and differed little from the normal. Thus in ankylosing spondylitis the abnormality is the opposite to that found in emphysema, that is, marked impairment of the M.I.F.R.

It is assumed that early involvement of the costovertebral joints in ankylosing spondylitis is the main cause of this phenomenon, and the authors suggest that this simple diagnostic test can be used as a sensitive adjunct to clinical assessment and radiology.
J. Warwick Buckler

COLLAGEN DISEASES

1503. **The Role of Antinuclear Reactions in the Diagnosis of Systemic Lupus Erythematosus: a Study of 53 Cases**
N. F. ROTHFIELD, J. M. PHYTHYON, C. MCEWEN, and P. MIESCHER. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] **4**, 223–239, June [received Aug.], 1961. 1 fig., 35 refs.

To assess the significance of antibodies to nuclei in systemic lupus erythematosus the authors, working at the New York University School of Medicine and Bellevue Hospital Center, New York, studied 53 patients with typical multi-system involvement; 38 in whom the L.E. cell test gave positive results (positive group) and 15 in whom the results were repeatedly negative (negative group). Antibodies to nucleoprotein, deoxyribose nucleic acid, and histone were detected by the sensitive conglutinin modification of the complement fixation test.

Renal, pulmonary, and central nervous system involvement, alopecia, conjunctivitis, and lymphadenopathy were commoner in the positive group, arthritis, skin rashes, pericarditis, vascular and peripheral nerve involvement, and psychosis occurred equally in both groups, while splenomegaly and arthritis deformans were commoner in the negative group. The incidence of anaemia, leucopenia, thrombocytopenia, and false positive Wassermann reaction was comparable in the two groups. Only 5 of the 38 in the positive group gave a negative response to the fluorescent test for antibodies

against nuclei compared with 5 of the 15 in the negative group. Antibodies against nucleoprotein occurred in 23 of the positive group and 6 of the negative group. The incidence of antibodies against deoxyribose nucleic acid was also lower in the negative group (4) than in the positive (18). The incidence of positive reaction in tests for the rheumatoid factor was similar in both groups and over 60% of patients with arthritis deformans gave a significant reaction in the inhibition reaction.

These results suggested that the two groups represented the same disease clinically, though members of the positive group tended to be more severely ill and have involvement of more systems. The incidence of a positive complement fixation reaction may have been related to the severity of the disease process; it was not related to renal or joint involvement. The authors conclude that the present concept of systemic lupus erythematosus may be too rigid owing to failure to consider the milder forms of the disease. Although repeated negative reactions for antibodies against nuclei make the diagnosis of systemic lupus erythematosus very unlikely, the mere absence of L.E. cells does not. A positive result in several tests for antibodies against nuclei makes the diagnosis more likely.

[See also Dörner *et al.*, *Dtsch. med. Wschr.*, 1961, **86**, 378 and 431; *Abstr. Wld Med.*, 1961, **30**, 233.]

G. L. Asherson

1504. **A Latex Nucleoprotein Test for Diagnosis of Systemic Lupus Erythematosus: a Comparative Evaluation**

E. L. Dubois, E. Drexler, and J. D. Arterberry. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **177**, 141–143, July 15, 1961. 1 fig., 8 refs.

The authors describe a simple slide test for systemic lupus erythematosus (S.L.E.) used at the Los Angeles County General Hospital (University of Southern California School of Medicine) and compare the results obtained with those of the L.E. cell test. One drop of a suspension of polystyrene latex particles coated with calf thymus nucleoprotein is mixed with one drop of serum or plasma and the mixture examined for macroscopic clumping. Tests were performed on 660 patients, including 154 in various stages of S.L.E. Positive results with this test were found in only 24 of 79 cases of S.L.E. in which the L.E. cell test gave a positive result. With the exception of 2 patients with rheumatoid arthritis and a positive L.E. cell reaction the latex test was negative in all patients with other diseases. Equivocal results, however, did occur, especially in patients with S.L.E.

M. Wilkinson

1505. **The Musculoskeletal Manifestations of Systemic Lupus Erythematosus**

M. Silver and O. Steinbrocker. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **176**, 1001–1003, June 24, 1961. 7 refs.

Over 7 years 35 patients with joint manifestations and a positive response to the L.E. cell test were seen in the Rheumatology Department of the Hospital for Joint Diseases, New York. Twelve of these patients had typical rheumatoid arthritis and no clinical features of systemic lupus erythematosus; 6 had clinical and laboratory features of late rheumatoid arthritis and systemic lupus erythematosus. In the remaining 17 patients the rheumatic symptoms varied in intensity with time. The response to corticosteroids was usually better than in rheumatoid arthritis, and progressive clinical and radiological joint changes were not seen. The pain was often disproportionate to the physical signs, and this may lead to an erroneous diagnosis of psychogenic rheumatism. Individual patients presented with intermittent synovitis with residual joint pain, persistent synovitis without cartilage destruction, migratory polyarthritis like rheumatic fever, and localized muscle pain suggesting dermatomyositis. All these patients had positive L.E. cell preparations, a serum globulin value above 3 g. per 100 ml., and a raised erythrocyte sedimentation rate, and nearly all had a haemoglobin level below 10 g. per 100 ml. Four had a false positive Wassermann reaction.

It is concluded that systemic lupus erythematosus may present as an obscure musculo-skeletal disorder.

G. L. Asherson

1506. **Clinical and Pathogenic Problems of Dermatomyositis.** (Вопросы клиники и патогенеза дерматомиозита)

B. N. Man'kovskii. *Журнал Невропатологии и Психиатрии* [*Ž. Nevropat. Psihiat.*] **61**, 543–548, No. 4, 1961. 2 figs., 18 refs.

The aetiology and pathogenesis of dermatomyositis, polymyositis, and other "collagen" diseases have not been clarified up to the present. The importance of an endocrine factor has been emphasized, especially in regard to the thyroid and adrenal glands, but this is obviously only a part of the process. Abnormal metabolism of vitamins (especially vitamin E) is also a factor, but again the cause of this is not clear. Infective processes too play a part, though attempts to establish a specific cause have been unsuccessful. A history of such infections (tonsillitis or other forms of streptococcal infection) was obtained in many of the present author's cases. It seems that the primary infection incites the development of an auto-allergy which persists in the absence of further external stimuli. The importance of the vegetative nervous system in the pathogenesis of dermatomyositis has not received much attention, although van der Lugt in 1955 suggested that the cause of the disease might be a dysfunction of the central vegetative mechanisms of the diencephalon which regulate tissue metabolism. Still less is known of the influence of these mechanisms upon the trophic state of connective tissue; it is noted that Elseyev in 1958 showed that stimulation of the hypothalamus increased the reaction of connective tissue to the injection of foreign substances.

The author then describes an almost complete cure in one patient with advanced dermatomyositis who received 4 courses of deep irradiation of the diencephalon given at intervals of 6 months; complete immobility gave place to free movement of all limbs and the disappearance of calcified areas in the muscles of the arms, legs, and pelvis. In another case 2 similar courses relieved the muscular dystrophy, but did not affect the calcified deposits.

L. Firman-Edwards

Physical Medicine

1507. **A Behavioural Investigation into Muscular Pain.** [In English]
L. J. Draspa. *Psychiatria et neurologia* [*Psychiat. et Neurol. (Basel)*] **141**, 367–380, June, 1961. 3 figs., 9 refs.

This is an attempt to show that some muscle pains (" fibrositis ") are due to muscle spasm. Patients with muscular pain were examined with particular reference to the location of the pain, the exact muscles involved, and the effect of passive relaxation in the relief of pain and of resisted movement in its reintroduction. In addition an assessment of muscle tension was made from passive movements of the affected parts, from active relaxation by the patient, by the patient's own rating of tenseness, and by other evidence of tension such as nail-biting. The number of patients examined was 112 (51 males and 61 females), mostly in the 40- and 50-year age groups.

It was found that in most cases there was a main muscle structure with severe pain and a second group of muscles in which pain was less severe. The commonest sites were the shoulder and neck (28 cases each). The affected muscles showed a variable degree of tenderness along their lengths, being often most sensitive at the musculo-tendinous junction; pressure on the tender area reproduced the spontaneous pain complained of, and this was further enhanced by forced isometric contraction. Treatment by passive relaxation removed the pain in a statistically significant number of cases; reintroduction of the pain could always be achieved by forced movement immediately after relaxation, but this became more difficult as relaxation improved. Pain could not be elicited in other muscles.

There is, in the figures given, a high correlation between tension and pain. The author suggests that " spasm " and tenderness occurring in chronic muscle pain are not generalized, but are probably in the distribution of a " motor unit " controlled by a single neurone.

B. E. W. Mace

1508. **Electrodiagnosis and Electrical Stimulation in the Treatment of Neuromuscular Disorders**
N. M. Liventsev. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **42**, 441–446, June, 1961. 9 figs.

This report from the State Research Institute of Balneology and Physiotherapy, Moscow, describes the muscle action potential. This is divided into an active phase and a restorative phase, the former consisting of the latent period and the spike. Reference is made to a critical point (the threshold), occurring at the end of the latent period, above which intensities of excitation cause contraction of the muscle. The form of the potential wave, the relative duration of the two principal phases, and the threshold value depend on the state of the nerve trunk and thus can be regarded as a measure of the degree of injury. The determination of these measurements carried out while varying the intensity, duration, and rate of rise of the single pulse is part of electrodiagnosis, but the author points out that the natural processes of excitation are rhythmic in character. Tetanic contraction of muscle depends on the frequency of electric pulses and gives an optimum or minimum contraction. By recording the effect of different frequencies on the neuromuscular unit the site and severity of nerve injuries can be studied. (Illustrative recordings are presented.) Details of various types of apparatus used in the U.S.S.R. for the electrodiagnosis of nerve injuries are given together with some results, which are compared with the operative findings.

It is stressed that electrotherapy must be based on the electrodiagnostic findings for which the correct duration, rate of rise, and frequency of electric pulse must be used. A rectangular pulse is stated to be more painful than an exponential pulse; the type and method of stimulation used in this study are described. It is claimed that the proper choice of pulses produces a tetanic contraction even in cases of " the light form of reaction of degeneration " and that if electrotherapy is combined with active exercises better results are obtained. *J. B. Millard*

1509. **Bedsores**
P. D. Bedford, L. Z. Cosin, and T. F. McCarthy. *Lancet* [*Lancet*] **2**, 76–78, July 8, 1961. 5 figs.

The mechanical alternating-pressure type of mattress designed to prevent dangerous pressure sores resulting in necrosis of muscle and subcutaneous tissue, and thus reducing nursing time, has been investigated at Cowley Road Hospital, Oxford. The mode of action of such appliances is described. The authors have experimented with a mattress having electrical contacts to show at what points the patient touches the bed during the air-pumping cycle; thus the " bottoming pressure " is determined. This interim study has shown that the appliances available at present do not yet meet all requirements, though the principle seems sound. Bottoming usually takes place on the sacrum, but prominent bony points like the elbow bottom at high pressures when allowed to take weight. Provided this is avoided, a pressure of 40 mm. Hg will keep any supine or prone patient clear of the bed. With the patient laterally placed or sitting, pressures up to 90 mm. Hg may be needed, depending on his weight. Obese subjects often have a wider distribution of weight and a low bottoming pressure. Correlations between body type and bottoming pressure were not close. With the patient sitting up at 90 degrees pressure under the ischial tuberosities rises very high, but it need not exceed 90 mm. Hg when a sitting angle of 60 degrees from the horizontal is used. This work emphasizes the risk which elderly patients run of developing pressure sores while sitting up. The alternating-pressure mattress is found to be most effective when placed on a resilient base. *J. N. Agate*

Neurology and Neurosurgery

1510. **Evaluation of EEG and Cortical Electrographic Studies for Prognosis of Seizures following Surgical Excision of Epileptogenic Lesions**
H. H. JASPER, G. ARFEL-CAPDEVILLE, and T. RASMUSSEN. *Epilepsia* [*Epilepsia* (*Boston*)] **2**, 130–137, June, 1961. 1 fig.

The prognostic value of pre- and postoperative electroencephalograms (EEGs) and electrocorticograms in patients with focal epileptic lesions treated by surgical excision has been investigated in 71 selected cases at the Neurological Institute and McGill University, Montreal. On a plus or minus basis—that is, good or bad prognosis from the EEG and satisfactory or poor clinical result—the EEG studies gave an accurate prognosis in 70 to 75% of cases, and on a four-category rating scale exact correspondence was found in 36 of the 71 cases. In exceptional cases a good clinical result was obtained in spite of a bad EEG prognosis and vice versa.

The authors conclude that repeated and detailed EEG studies are of definite value in assessing prognosis after surgical treatment in selected cases of focal epilepsy.

J. B. Stanton

1511. **Intrathecal Tuberculin in Disseminated Sclerosis: a Controlled Trial**
R. E. KELLY and E. H. JELLINEK. *British Medical Journal* [*Brit. med. J.*] **2**, 421–424, Aug. 12, 1961. 3 refs.

A trial of intrathecal tuberculin (P.P.D.) was made on 20 patients with disseminated sclerosis in whom the disease seemed active and in whom new episodes of demyelination or deterioration were anticipated. On comparing their fate with a group of 20 carefully matched control cases we conclude that intrathecal tuberculin in disseminated sclerosis is a form of treatment which confers no benefit on the patient, despite the unpleasantness of the reaction and the length of the stay in hospital. Indeed, we are not satisfied that it may not lead to reactivation of the condition during the month after the treatment.

We hope that trials like ours and the similar results of Miller *et al.* will prevent the use of P.P.D. as a placebo in a condition where there is great pressure for some active form of treatment. Other untested and potentially harmful methods such as intravenous "pyrifer", or arsenic and bismuth, should similarly be abandoned for truly harmless placebos.—[Authors' summary.]

1512. **Ergometry in the Diagnosis of Myasthenia Gravis**
R. GREENE, D. F. RIDEOUT, and M. L. SHAW. *Lancet* [*Lancet*] **2**, 281–284, Aug. 5, 1961. 6 figs., 2 refs.

The authors have carried out a study at the New End Hospital, London, on 54 subjects using the Osserman modification of the Schwab-type ergograph. This apparatus records the force exerted by squeezing a rubber bulb, the pressure being transmitted along undistensible polythene tubing to a cylinder containing a spring-loaded piston connected to an arm carrying an ink recording device. The deflection of the arm bears a constant relation to the force exerted. The recording paper moves at a constant rate and the mechanism causes a hammer to strike a bell every second. The subjects were instructed to hold the rubber bulb in the palm of the hand, to squeeze it as hard as possible at each stroke of the bell, and to relax the grip completely after each squeeze. A record of the rate of fatigue is given by the upper points of the tracing, and the authors have attempted to represent this numerically as a factor termed the half-fatigue time. Of the 54 subjects, 13 adults and 1 child were normal, while 12 had myasthenia gravis, 19 muscular dystrophy, 1 amyotonia congenita, 3 residual paresis after poliomyelitis, 1 myxoedema, 2 thyrotoxic myopathy, 1 thyrotoxicosis without myopathy, and 1 cervical spondylosis.

The authors consider that a definite diagnosis of myasthenia gravis can be based upon a half-fatigue time of less than 50 seconds. With values of 50 to 80 seconds the occurrence of rapid fatigue shown by pen immobility in less than 100 seconds or a ratio of greatest to final height between 5:1 and 30:1 is also diagnostic. Patients with muscular weakness due to causes other than myasthenia have a half-fatigue time greater than that of normal individuals. The authors consider that use of the ergograph provides an excellent screening test in cases of muscular weakness and that it is particularly useful in confirming the diagnosis of myasthenia gravis.

Kenneth Tyler

BRAIN AND MENINGES

1513. **Post-traumatic Amnesia in Closed Head Injury**
W. R. RUSSELL and A. SMITH. *Archives of Neurology* [*Arch. Neurol.* (*Chicago*)] **5**, 4–17, July, 1961. 1 fig., 14 refs.

The authors have analysed data from 1,766 cases of closed head injury referred to the Military Hospital for Head Injuries, Oxford, during World War II, in order to correlate the clinical features with the duration of post-traumatic amnesia (P.T.A.), which is defined as "the length of the interval during which current events have not been stored". From this total, 442 cases were rejected because of focal brain injury or serious injury to other parts of the body. The remainder were divided into 5 groups according to the duration of P.T.A. (*nil*, less than 1 hour, 1 to 24 hours, 1 to 7 days, and more than 7 days).

Analysis of the present data according to age group, together with a similar analysis of 1,000 consecutive civilian cases, confirmed previous findings that the duration of P.T.A. increases with age. It was also shown that for any given duration of P.T.A. the incidence of

certain sequelae rises with age. Consideration of 100 different signs and symptoms permitted their division into 2 groups. One, designated "organic" and including fractured skull, anosmia, dysphasia, retrograde amnesia of more than 30 minutes' duration, memory and/or calculation defect, and motor disorder, showed a systematic increase in incidence with increasing duration of P.T.A. and age. The other, designated "non-organic" and including anxiety and depression, headache, and dizziness, showed no correlation with increasing P.T.A. and age. The percentage of men invalided from military service showed a consistent positive correlation with the duration of P.T.A.

The authors suggest that in the classification of cases of closed head injury without signs of focal damage the duration of P.T.A. provides the most sensitive and reliable index of severity, particularly when the age of the patient is taken into account.

[This valuable and important paper deserves to be read in the original.] *B. S. Meldrum*

1514. **Head Injuries in Car Accidents Treated at the Leningrad Hospitals during the Year 1958.** (Повреждение головы по данным больниц Ленинграда за 1958 г)

G. D. Lučko. *Советская Медицина* [*Sovetsk. Med.*] **25**, 96–99, Aug., 1961. 1 fig.

This is a comparative study of head injuries due to car accidents treated at the Leningrad hospitals during the years 1934–9, and during the year 1958. The various types of head injury, their incidence, and the mortality according to age and sex are analysed. The mortality from head injuries during 1958 was lower than in 1934–9. The proportion of car accidents involving drunken drivers in 1934–9 was 44·8% of the total, and nearly one-third of these drivers had head injuries. In 1958 the proportion of head injuries among drunk drivers fell to about one-sixth. *A. Orley*

1515. **Survival after Non-haemorrhagic Cerebrovascular Accidents: a Prospective Study**

J. Marshall and A. C. Kaeser. *British Medical Journal* [*Brit. med. J.*] **2**, 73–77, July 8, 1961. 5 figs., 12 refs.

In this prospective study, which supplements the retrospective one carried out by the senior author with Shaw (*Brit. med. J.*, 1959, **1**, 1614; *Abstr. Wld Med.*, 1960, **27**, 60), 177 patients (122 males) who had recovered from a non-embolic cerebral infarction have so far been kept under review, being examined at 4-weekly intervals for up to 3 years at the National Hospital, Queen Square, London. Of these, 89 were treated with anticoagulants, but this treatment was subsequently withdrawn in 18 cases because of hypertension. The data on prognosis in this study were therefore based on the course of 106 patients, that is, 88 who did not receive anticoagulant drugs plus the 18 from whom this treatment was withdrawn.

At the end of one year 94% of these 72 male and 34 female patients were alive, and after 2 years 85% of males and 89% of females were still alive. The survival rates at 2 years for the two subgroups of patients under and over the age of 60 were 88% and 83% respectively, compared with 86 and 75% respectively for the 71 patients treated with anticoagulants. This finding supports the belief that anticoagulant therapy is not beneficial, and may indeed be hazardous, in patients aged over 60. The survival rates at 2 years for patients with diastolic blood pressure below and above 110 mm. Hg were 96 and 75% respectively. In patients with electrocardiographic evidence of myocardial ischaemia or left ventricular hypertrophy the 2-year survival rate was 66% compared with 96% for those with a normal electrocardiogram. In regard to other factors, it was found that the survival rate was not significantly affected by the site of the lesion, the serum cholesterol level, or the number of incidents of infarction. However, the number of previous incidents was related to the frequency of subsequent non-fatal attacks, as was shown by the fact that of 84 patients who had experienced only one episode before coming under observation, only 8 suffered a subsequent attack during the 2-year period, whereas of 22 patients who had had more than one attack, 7 did so. Among the 28 patients who died the cause of death was cerebrovascular in 13 and cardiac in 11. Only 2 of the whole series of 177 patients had transient repeated ischaemic episodes, and these were unaffected by anticoagulant therapy.

The authors stress the adverse effect on prognosis of a high blood pressure and of electrocardiographic signs of left ventricular hypertrophy or of ischaemic heart disease. They also propose the concept of "active" and "inactive" cerebrovascular disease, the former being associated with a tendency to recurrent, non-fatal, episodes. *Bernard Isaacs*

1516. **Primary Intracerebral Haemorrhage: a Controlled Trial of Surgical and Conservative Treatment in 180 Unselected Cases**

W. McKissock, A. Richardson, and J. Taylor. *Lancet* [*Lancet*] **2**, 221–226, July 29, 1961. 3 figs., 4 refs.

From St. George's Hospital, London, is reported a controlled trial of the influence of surgical treatment on the mortality and morbidity of primary intracerebral haemorrhage. The diagnosis of cerebral haemorrhage was established by clinical examination, lumbar puncture, and cerebral angiography. Patients with hindbrain haemorrhage, those who died before full investigation, those who recovered very rapidly, and those in whom the diagnosis was in doubt were omitted from the series. Of the 180 patients included in the trial, 91 were allocated at random to a "conservative management" group and 89 were selected for surgery.

The groups were found to be closely comparable in those factors known from previous experience to affect prognosis, that is, age, level of blood pressure, state of consciousness, and angiographic midline displacement. The over-all mortality within 6 months of onset was 51% in the group treated conservatively and 65% in that given surgical treatment. Analysis of the results revealed only one small group in which the results of surgery appeared to be better than those of conservative management—namely, women with normal blood pres-

sure; but the numbers were too small to allow of firm conclusions. In all other groups patients treated surgically fared worse than those managed conservatively, notably the group of hypertensive women without angiographic displacement, in whom the mortality after conservative management was 24% and after surgical treatment 82%.

The study also revealed the following facts about the natural history of cerebral haemorrhage. The commonest site of haemorrhage was the external capsule. The mortality among hypertensive females was only half that of hypertensive males, and the mortality rate was higher in normotensive than in hypertensive patients. Up to the age of 70 increasing age did not materially worsen the prognosis. The level of consciousness 24 hours after the stroke was a valuable guide to the outcome.

[This very important study should be read in full.]

Bernard Isaacs

1517. **Posterior Cerebral Artery Occlusion: a Clinical and Angiographic Study**

R. J. MONES, N. CHRISTOFF, and M. B. BENDER. *Archives of Neurology* [*Arch. Neurol.* (*Chicago*)] **5**, 68–76, July, 1961. 4 figs., 13 refs.

This study from the Mount Sinai Hospital, New York, correlates the results of vertebral angiography with the neurological findings in 106 consecutive cases in order to determine the clinical significance of non-filling of one or both posterior cerebral arteries (P.C.A.). The retrospective diagnoses were basilar artery disease (32 cases), tumours (30), subarachnoid haemorrhage (19), and unknown disease of the brain (26) [making 107 cases].

Non-filling of one P.C.A. on vertebral angiography was seen in 12 patients. Four of these had homonymous visual field defects corresponding to the non-filled P.C.A.; carotid angiography did not lead to filling in these cases. Carotid angiography was performed on 3 of the 8 patients without visual field defects and revealed filling of the previously non-filled P.C.A. in all. Bilateral non-filling of the P.C.A. on vertebral angiography was seen in 6 patients. All had evidence of brain-stem dysfunction; one had cerebral blindness, and the other 5 had homonymous visual field defects (bilateral field defects in 2 cases and hemianopsia, inferior quadrantic defect, and paramacular scotoma in one each). Of 51 patients with bilateral filling of the P.C.A. who had adequate visual field examinations, 15 had homonymous visual field defects. Of these, 3 had neoplasm, one had internal carotid artery occlusion, 6 had clinical evidence of basilar artery disease but normal vertebral arteriograms, and 5 remained without aetiological diagnosis.

It is concluded that unilateral non-filling of the P.C.A. on vertebral angiography calls for ipsilateral carotid angiography. The authors suggest that confirmation of non-filling indicates occlusive disease. Non-filling of both posterior cerebral arteries is associated with clinical evidence of brain-stem and occipital lobe disease.

[The table of diagnostic categories is inaccurate and inconsistent with the text. The suggestion that confirmed unilateral non-filling indicates occlusive disease is weakened by the absence of post-mortem studies (especially as no occlusion was found in one of the 2 patients with bilateral non-filling who were examined post mortem) and by the lack of information about the carotid angiograms of the patients with tumours.]

B. S. Meldrum

1518. **The Treatment of Cerebral Aneurysms by Ligation of the Common Carotid Artery**

M. SCOTT and E. SKWAROK. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **113**, 54–61, July, 1961. 27 refs.

This paper is another contribution to the controversy as to whether or not intracranial surgical intervention is better than ligation of the carotid vessels in the neck in the treatment of cerebral aneurysm. At Temple University Medical Center, Philadelphia, 31 patients with berry aneurysms were treated by carotid ligation; their ages ranged up to 71 years, and over one-third were hypertensive. Before ligation 21 were alert, 4 were drowsy, and 6 unconscious; 4 of the postoperative deaths were in this last group. The Matas test was not performed, but patients were observed for 15 to 30 minutes after temporary complete ligation of the carotid artery before the incision was closed. There were 5 postoperative deaths (16%) and postoperative sequelae in 8 cases (26%).

Of 21 patients who were followed up for a maximum period of 11 years, 4 died of subsequent rupture of the aneurysm 1 to 5 years after ligation. [The authors do not correlate the results of this form of treatment with the position of the aneurysm], but they conclude that in cases of aneurysm of the internal carotid or posterior communicating arteries the results of carotid ligation compare favourably with those obtained by intracranial intervention. In their experience ligation of the carotid artery is contraindicated if (1) the patient cannot tolerate temporary occlusion of the vessel; (2) the blood pressure is low or alternatively if there is severe hypertension; (3) the patient is in stupor or coma; (4) no collateral circulation can be demonstrated by angiography with cross compression; and (5) the clinical or angiography findings suggest that a direct attack on the aneurysm is required.

J. V. Crawford

1519. **Cerebral Infarction: the Role of Stenosis of the Extracranial Cerebral Arteries.** [Monograph]

P. O. YATES and E. C. HUTCHINSON. *Medical Research Council. Special Report Series* [*Spec. Rep. Ser. med. Res. Coun.* (*Lond.*)] No. 300, 1–95, 1961. 20 figs., bibliography.

1520. **History, Clinical Findings, and Course of Glioblastoma Multiforme.** (Anamnese, Klinik und Katamnese des Glioblastoma multiforme)

U. VOGT. *Nervenarzt* [*Nervenarzt*] **32**, 297–301, July, 1961. 4 figs., 9 refs.

In this study from the Neurosurgical and Neurological Clinics of the Free University, Berlin, the author reviews 250 histologically proven cases of glioblastoma multiforme. The duration of symptoms was mostly less than 6 months, and on admission to hospital over 50% of patients had marked neurological deficit, 62% having

bilateral papilloedema. In 26·6% of cases no surgical treatment was possible and in 24% only needle biopsy or subtemporal decompression could be performed. Total or partial resection of the tumour was carried out in 47·6% of cases, deep x-ray therapy in 25%, and radioactive cobalt implantation in 5·4%. Radical removal of the tumour followed by deep x-ray therapy was found to give the longest survival rates (6 to 30 months, or longer in 2 cases). In 30% of cases the patient was able to return to work for a variable period of time after treatment. *H. S. Schutta*

EPILEPSY

1521. **Psychomotor Epilepsy in Childhood. Parts I and II.** (Die psychomotorische Epilepsie im Kindesalter. I. und II. Mitteilungen)
A. MATTHES. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **85**, 455–492, 1961. 16 figs., bibliography.

In the first part of this paper the author surveys the clinical features in 135 children aged 2 to 14 years with " psychomotor epilepsy ". In a short review of the relevant literature he discusses the various alternative names which have been applied to this form of epilepsy and gives his reasons for avoiding the term " temporal lobe epilepsy ". The 135 patients formed part of a series of 643 patients seen at the University Children's Clinic, Heidelberg, suffering from epilepsy of all types. Psychomotor epilepsy was only slightly more common in girls (54% of the total) and there was no sharp peak of incidence at any particular age, in contrast to petit mal. The psychomotor attacks had a wide symptomatology which often varied from one attack to another in the same patient. Auras occurred in nearly 60% of the patients, the most frequent being a sensation of abdominal discomfort, but the common olfactory, gustatory, visual, and auditory hallucinations and the classic " dreamy state " were seldom encountered in these children. Automatisms, particularly snorting, smacking of the lips, and licking and swallowing movements, accompanied the attacks in 81% of cases, and reddening or pallor of the face was another common feature. While the majority of the children felt exhausted or fell asleep after an attack, one-third were able to continue immediately with their previous activity. The duration of attacks ranged from 20 seconds to 25 minutes in different patients, but there were also wide variations in the duration of attacks in the same patient. The incidence of individual symptoms observed in 224 attacks is shown in tabular form.

The second part of the paper reports the ictal and interictal electroencephalographic (EEG) findings in these patients. With the aid of serial recordings and of activation techniques, positive interictal records were obtained in 88% of the cases. Focal spikes or focal slow waves were seen in the records of 121 of the 135 patients, a generalized abnormality in 9 cases, and a normal record in 5. In 81% of the cases the focal abnormalities were located in the temporal lobes. In 49 cases an attack was observed during the EEG recording, the majority being provoked by activation—usually hyperventilation. Only a minority of the recordings showed a clear-cut focal origin for the epileptic discharge. The physical examination of the 135 children revealed that 18 had a dysplastic habitus, while in 19 there were neurological abnormalities suggesting a cerebral lesion. Pneumoencephalograms obtained in 53 patients showed the presence of ventricular abnormalities in 42 (81%). The author describes the disturbance of intellect, behaviour, and personality observed in these children, but notes that only 3 of them could be regarded as definitely psychotic. *J. B. Stanton*

1522. **The Relations between Olfactory and Vestibular Sensory Impulses and Temporal Lobe Epilepsy.** [In English]
V. IONĂŞESCU. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. scand.*] **36**, 415–426, 1961. 5 figs., 22 refs.

The author of this paper from the Institute of Neurology, Bucharest, describes a case of epilepsy in which olfactory hallucinations ceased to form part of the attacks after damage to the olfactory tracts during a neurosurgical operation. He also draws attention to an analogous case in the literature in which visual hallucinatory seizures ceased after the patient became blind following a gunshot wound of the optic chiasma.

The effect of olfactory and vestibular stimulation in activating the electroencephalogram (EEG) was studied in patients with temporal lobe epilepsy. Positive results were obtained in 5 out of 25 patients by vestibular stimulation (cold caloric test), and in 5 out of 35 patients by olfactory stimulation. The positive results were nonspecific, however, and produced EEG modifications not in patients with uncinate or vestibular fits, but in patients with auditory and visual hallucinatory seizures or with psychomotor epilepsy. In 2 patients there was a response to both types of stimulation. The mode of action of the stimuli is presumed to be through collaterals to the reticular formation. *J. B. Stanton*

1523. **Incidence of Post-traumatic Epilepsy**
W. F. CAVENESS and H. R. LISS. *Epilepsia* [*Epilepsia (Boston)*] **2**, 123–129, June, 1961. 1 fig., 7 refs.

The authors review previous studies on the incidence of post-traumatic epilepsy, including experience in both world wars, and report their own survey of head injuries in the U.S. Armed Services during the Korean war. Six categories indicating three degrees of severity each of penetrating and closed head injuries are employed. In one-quarter of the most severe cases of closed head injury and one-half of the most severe cases of penetrating injury epilepsy developed, the incidence decreasing to 8·5% in the mildest closed injuries. The form of the attack was a major convulsion in over one-half of cases. Three-quarters of the patients developing post-traumatic epilepsy had their first seizure within one year of the injury. Generally speaking the earlier the onset of seizures after injury, especially if within the first 14 days, the more likely is spontaneous cessation of the seizures to occur and vice versa. *J. B. Stanton*

Psychiatry

1524. **Obsessional Illness in Mental Hospital Patients**
I. M. INGRAM. *Journal of Mental Science* [*J. ment. Sci.*] **107**, 382–402, May [received July], 1961. 31 refs.

The natural history of obsessional illness has been studied in 89 mental hospital in-patients. Diagnostically 37 were classified as obsessive-compulsive neurosis, 16 as phobic-ruminative, 14 were doubtfully schizophrenic, 10 showed depressive features and 12 were otherwise atypical. The incidence was 0·9% of all admissions. The celibacy rate was 51%, the fertility rate 1·1%. Social class and intelligence were higher than in control groups of hysterics and anxiety states. Childhood symptoms were seen in 36%, precipitants of the illness were important in 69%. Pregnancy was a common precipitant. The illness began early (mean 24·7 years) but admission was delayed (mean age 36·1 years). The majority (54%) showed a constant course; only 13% a definitely phasic one.

Sixty-four cases, 18 of whom were leucotomized, were followed up for an average of 5·9 years. Of those not leucotomized 39% were improved; and 66% were working. Of those leucotomized, 55% were improved and 72% working. In the typical obsessive-compulsive cases only one of the 16 not leucotomized was improved, compared with 7 of the 13 leucotomized.

Spontaneous improvement was significantly associated with atypicality, absence of motor symptoms, absence of childhood symptoms, and a short duration prior to admission. It was concluded that chronicity and presence of motor symptoms were not contra-indications for leucotomy and that many of the current recommendations for leucotomy are indicators of spontaneous remission. Spontaneous recovery in severe obsessional illness is rare, improvement common, and disablement only occurs in a minority.—[Author's summary.]

1525. **Psychiatric Headache: a Clinical Study**
N. L. GITTLESON. *Journal of Mental Science* [*J. ment. Sci.*] **107**, 403–416, May [received July], 1961. 37 refs.

All patients suffering from psychogenic headache, alone or with other symptoms, who were admitted as in-patients over a 2-year period to the Psychiatric Unit of the University of Manchester were studied. Patients with migraine or organic brain disease were excluded.

The group comprised 19 male and 34 female patients. The patients suffering from headache were compared with all the other patients, 69 males and 117 females, admitted to the Unit over the same period except for patients with organic brain disease. Amongst the female patients the headache group contained a significantly higher proportion of patients classified as suffering, alone or in combination with a psychosis, from an insecure personality disorder (which corresponds to the anankastic or sensitive obsessional personality disorder).

Within the headache group the pattern of headache was strikingly constant amongst the various diagnostic and personality groups. The pattern was that of a constant bilateral frontal pressure. It is tentatively postulated that " psychiatric headache " is perhaps a preformed mechanism which can be triggered by many stresses. This study suggests that female sufferers from an insecure personality disorder are more likely to possess this mechanism than those possessing other personality structures. They are also more likely to consider the headache as being caused by " nerves ".

It was found that the prognosis of the headache was that of the underlying psychiatric condition.—[From the author's summary.]

1526. **On the Communications of Suicidal Ideas. II. Some Medical Considerations**
P. G. YESSLER, J. J. GIBBS, and H. A. BECKER. *Archives of General Psychiatry* [*Arch. gen. Psychiat.*] **5**, 12–29, July, 1961. 2 figs., 8 refs.

In the first part of this investigation, carried out at the Walter Reed Army Institute of Research, Washington, D.C., the authors studied the records of 272 cases of suicide and 104 of attempted suicide to ascertain whether there were any differences between the histories of those who communicated their suicidal intention and those who did not, a " communicator " being defined as one who had shown evidence of trying to convey verbally his intention to others before committing the act. They found that in 29% of suicides and 25% of attempted suicides such communication had been made, the difference not being significant. The majority of suicides occurred in psychotic and neurotic subjects, whereas attempts at suicide were overwhelmingly among those with character and behaviour disorders. The authors assessed the " mental status " of the subjects from the opinions of doctors, friends, and associates and on this basis classified them into such categories as depressed, reserved, anxious, perfectionist, or immature. Suicide occurred most frequently in the depressed and morose group and attempted suicide in the immature group. Of the whole group, 29·8% had communicated their intention, 54·8% of the " immature passive-aggressive, stubborn " subjects doing so compared with 18·1% of the " quiet, shy, reserved " subjects. But when some of the groups were combined most of these differences disappeared.

The subjects' last medical contacts, both psychiatric and other, were then examined (those taking place more than a year before the suicidal act being excluded) since it was considered that medical contacts could have a significant bearing on the subject's communication or otherwise in that a consultation might represent a " cry for help " and be a concealed suicidal communication. A high proportion of the subjects had sought medical advice shortly before the act, but there was no difference between the two groups—thus 84·6% of suicides and 82·7% of attempted suicides had consulted a doctor

within 6 months and 33·3% and 46% respectively within a week before the act. The shorter the time between consultation and the act, the greater was the frequency of communication; consultations more than 6 months before the act had no relevance. Of non-communicators who had non-psychiatric contact within a year, in only 14·8% of cases could it be said that there was no connexion with the suicide; 63% of these had shown worry, in some cases irrational, over the illness which brought them to the doctor. This degree of concern, coupled with the proximity to the suicidal act, suggests that the consultation was a means of calling attention to the state of distress. Of communicators who had sought a non-psychiatric consultation, 75% showed no concern about their physical condition. It was concluded that 50% of all communicators seen psychiatrically came for reasons directly connected with suicide, whereas among non-communicators this proportion was only 17·4%. Communicators are likely to call attention to themselves by other behaviour which causes their associated anxiety and are referred for this reason; only 16·5% saw the psychiatrist of their own volition. The authors suggest that non-communicators may use medical contacts as a hidden way of drawing the attention of others to their emotional plight. *Gavin Thurston*

1527. **Physiological Patterns: a Diagnostic Test Procedure Based on the Conditioned Reflex Method**
T. BAN and L. LEVY. *Journal of Neuropsychiatry* [*J. Neuropsychiat.*] **2**, 228–231, June, 1961. 1 fig., 6 refs.

This paper from the Allan Memorial Institute (McGill University), Montreal, describes a method that may prove to be of value in measuring clinical change in psychiatric patients, none of the current methods hitherto available having proved entirely satisfactory. The procedure is based on the eye-blink conditioned reflex technique, the stimulus being a puff of air and the conditional stimulus a tone of 400 or 1,000 c.p.s. Pavlov originally described 8 physiological parameters to conditioned reflexes and these, which were studied and evaluated over 5 days in 10 human subjects, are described and illustrated in recordings reproduced. The formation of such reflexes is discussed with reference to the brain-stem reticular formation. It is hoped that when applied to psychiatric patients the method will provide results that can be used as an objective measure of change in psychological functioning. *B. M. Davies*

1528. **A Comparative Trial of Four Mono-amine Oxidase Inhibitors on Chronic Depressives**
T. J. N. BATES and A. D. MCL. DOUGLAS. *Journal of Mental Science* [*J. ment. Sci.*] **107**, 538–546, May [received July], 1961. 18 refs.

A comparative trial of 4 well-known antidepressive drugs, all monoamine oxidase inhibitors, is described from Saxondale Hospital, Nottingham. A total of 63 patients with chronic depression who had failed to respond to other treatments and had a history of at least one year took part. The drugs were "cavodil" (β-phenyl*iso*propyl hydrazine hydrochloride), "marsilid" iproniazid), "nardil" (phenelzine), and "niamid" (nialamide), and the trial was conducted so as to use all 24 possible arrangements of the 4 drugs (the "latin-square" technique). Patients were given each drug for 5 weeks with a 2-week interval between treatments. Assessment was recorded on a rating scale of 14 depressive symptoms.

The results failed to show any clear-cut indications as to the type of depression which would be benefited by a particular drug. The 50 to 60 age group showed a better response generally than other age groups. The only symptom that was significantly associated with successful treatment was "accentuation of symptoms in the morning". Insomnia and anxiety were generally not relieved, and in some cases these symptoms were aggravated. Of the different categories of depression, the "atypical" depressions tended to do better than other types. Sex, duration of symptoms, and whether an in-patient or out-patient were not significant factors. The drugs appeared of value in the following order: nardil, niamid, marsilid, and cavodil. Niamid appeared better for patients under 40 years. In the over-50 age group nardil was significantly better than marsilid. There was a trend for nardil to succeed more often in the retarded and atypical depressions and for niamid to succeed more often in the neurotic depressions. Improvement was apparent usually by the second week of treatment. Elation and hypomania were not uncommon side-effects. An acute confusional state occurred with nardil. Marsilid produced the greatest number of minor side-effects. *J. S. Bearcroft*

SCHIZOPHRENIA

1529. **"Rheumatic" Schizophrenia: an Epidemiological Study**
N. M. WERTHEIMER. *Archives of General Psychiatry* [*Arch. gen. Psychiat.*] **4**, 579–596, June, 1961. 36 refs.

In this paper from the University of Colorado the author first points out that rheumatic fever can involve the nervous system, chorea being the most commonly recognized form of such involvement. From a study of 2,658 case histories of schizophrenic patients in three different State hospitals she then suggests that some of them had a rheumatic brain involvement. In some this was recognized by a previous history of overt rheumatic disease, while in others with no such history evidence of this aetiology could be adduced from symptoms reminiscent of chorea, such as grimacing and twitching. When the "rheumatic group" was compared with schizophrenic patients with no apparent rheumatic aetiology certain differences appeared, the rheumatic group showing the following tendencies: a non-paranoid illness, an early age of onset of the illness, an insidious or recurrent course, and a poor outcome.

Further evidence of a rheumatic aetiology in schizophrenic patients who grimace is suggested by other observations, which may be regarded as equivalents of late or pubertal chorea. Thus (1) grimacing schizophrenia occurs more commonly in males, whereas pubertal chorea is commoner in females; (2) when schizophrenia

is associated with a history of previous rheumatic illness grimacing is usually seen in patients whose initial rheumatic attack had occurred in puberty; (3) the seasonal pattern of admissions is similar for both acute grimacing schizophrenia and the pubertal type of chorea; (4) an excess of first-born children is found in both female choreics and grimacing schizophrenic males, suggesting perhaps that their position in the family protected these children from early exposure to streptococcal infections and so delayed rheumatic symptoms until susceptibility to brain involvement was hypothetically more likely. Some evidence is also available that "rheumatic" schizophrenia may be more common in areas with a high rate of streptococcal infection. Both schizophrenia and rheumatic fever are found in association with a low socio-economic level in the general population, but in the group of schizophrenic patients alone no particular relationship between rheumatic fever and socio-economic level was apparent, suggesting a common aetiological factor for both. *J. S. Bearcroft*

1530. **Treatment of Schizophrenia in General Hospitals**
P. ROHDE and W. SARGANT. *British Medical Journal* [*Brit. med. J.*] **2**, 67–70, July 8, 1961. 4 refs.

In 1950 a psychiatric ward was opened at the Royal Waterloo Hospital, London, consisting of single and double rooms for 20 patients of both sexes, a day room, and a dining room. The ward remained unlocked so that suitable patients could mix with those from other wards. In the first 10 years 95 schizophrenic patients were selected for admission who had a median age of 32 years and a median length of illness of 2 years and 2 months. Chronic deteriorated patients had to be excluded and the same applied, before the introduction of chlorpromazine in 1956, to severely disturbed patients. In spite of this selection of suitable patients, 31% had to be transferred to mental hospitals before 1956 and 9% since. A follow-up of these 95 patients was complete except in 4 cases; these 4 patients were regarded as living in the community, but still psychotic. Four patients had died, 2 of them through suicide; 56 (59%) had had temporary relapses, but 82 (86%) were out of hospital at the time of the follow-up; 46 (48·5%) were symptom-free and 25 (26·5%) had residual symptoms.

Before 1956 treatment consisted mainly in insulin coma and electric convulsion therapy (E.C.T.). Since then patients have been treated with 300 mg. of chlorpromazine a day at first, gradually increasing to a maximum of 1,400 mg., if necessary, and then being reduced to the minimum dose required. A maintenance dose is continued after discharge. E.C.T. is started as soon as possible after admission and is given 2 to 3 times a week at first. Modified insulin therapy is sometimes given to underweight patients. The average length of stay of patients has fallen since 1956 from 10·7 to 6·3 weeks. There has also been a great improvement in the therapeutic results since then. The social and psychiatric status 2 years after discharge of 2 groups of comparable patients, one admitted before and the other after 1956, was studied. There were 39 patients in each group. Of the pre-1956 group, 20 (51%) were still psychotic compared with only 8 (20%) of the post-1956 group. Of the former group, 12 (31%) were still in hospital compared with 2 (5%) of the latter.

Although these results were achieved in a selected group of patients, they are regarded as evidence of the superiority of the modern chlorpromazine–E.C.T. treatment over the previous treatment with insulin coma and E.C.T. *F. K. Taylor*

1531. **Controlled Trial of Prochlorperazine ("Stemetil") in Schizophrenia**
SOUTH-EAST REGION (SCOTLAND) THERAPEUTIC TRIALS COMMITTEE. *Journal of Mental Science* [*J. ment. Sci.*] **107**, 514–522, May [received July], 1961. 22 refs.

In this regional study carried out at three hospitals in south-east Scotland under the auspices of the Department of Psychological Medicine of the University of Edinburgh the 112 chronic schizophrenic patients, 54 male and 58 female, selected for the trial were divided into two matched groups, the aim being to compare the effects of prochlorperazine, chlorpromazine, and a placebo, each given for a period of one month. After being stabilized on chlorpromazine the patients were transferred to either prochlorperazine or a placebo, the usual double-blind, cross-over method being employed. The dosage was determined by the stabilizing dose of chlorpromazine in the initial period. Weekly rating scales were completed for each patient, comprising 18 items relating to behaviour and mental state. In addition, a structured interview based on symptoms was independently recorded after each treatment period.

The results did not suggest that prochlorperazine was of particular value in the treatment of chronic schizophrenics. The 24 patients who did improve did not differ significantly on any of the 22 different factors studied from the trial group as a whole, except that they included a disproportionate number of paranoid patients. An interesting finding was the improvement recorded in more than one-quarter (26·5%) of the patients when they were transferred to the placebo. *J. S. Bearcroft*

TREATMENT

1532. **The Effectiveness of Psychotherapy Alone and in Conjunction with Perphenazine or Placebo in the Treatment of Neurotic and Hyperkinetic Children**
L. EISENBERG, A. GILBERT, L. CYTRYN, and P. A. MOLLING. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **117**, 1088–1093, June, 1961. 11 refs.

In a previous double-blind study the authors found no evidence that either meprobamate or prochlorperazine was superior to a placebo in treating disturbed children receiving concurrent psychotherapy. Whatever the medication, the outcome was better for children defined as neurotic ("cases in which the manifestations of, or defences against, anxiety were predominant") than for children defined as hyperkinetic ("overactive, distractible, non-conforming, disturbing to others, but showing little or no anxiety"); children showing sociopathic behaviour were not included.

The present study from Johns Hopkins Hospital, Baltimore, follows this up by comparing the response in the two diagnostic groups to three randomly assigned treatment schedules: (*a*) psychotherapy without medication; (*b*) psychotherapy plus placebo; and (*c*) psychotherapy plus perphenazine (8 to 16 mg. daily). Psychotherapy consisted in initial evaluation by social worker and psychiatrist of parent and child respectively, followed by 4 half-hour sessions over 11 weeks for parent and child. Improvement was rated on reports from mother and school and the psychiatrist's assessment of the child. The investigation covered 33 neurotic and 23 hyperkinetic children.

The contrast in outcome between the two diagnostic groups was confirmed. There was, however, no difference in outcome between the three treatment groups except a tendency for the hyperkinetic patients to do better on treatment (*c*) than the other regimens. [The numbers in each group were very small.]

The failure of the hyperkinetic group to respond to psychotherapy may reflect a fairly high percentage of children with cerebral pathology in this group. Such children are less likely to be accepted for treatment in a psychotherapeutically orientated clinic, and the authors stress the need for exploration of alternative modes of treatment for them and a less conservative outlook on pharmacological aids to treatment in child-guidance clinics. They conclude that short-term psychotherapy appears to be no less effective than long-term psychotherapy and that the latter has the disadvantage of fostering dependency and maintaining a morbid focus on pathology over a long period.

The authors are at present planning an investigation to assess the expectation of spontaneous remissions in an untreated control group of neurotic children.

Christopher Wardle

1533. **Clinical Trial of a New Sedative Antidepressant, 7162 RP, a Derivative of Iminodibenzyl.** (Un nouvel antidépresseur sédatif dérivé de l'iminodibenzyle: le 7162 RP)

P. A. LAMBERT and J. GUYOTAT. *Presse médicale* [*Presse méd.*] **69**, 1425–1428, June 24, 1961. 16 refs.

There are two recognized types of antidepressant drug, namely, monoamine oxidase inhibitors and drugs resembling imipramine or derived from an iminodibenzyl nucleus. One of the latter type is 7162 RP, a new antidepressant drug with sedative or tranquillizing properties. Its chemical formula contains the iminodibenzyl nucleus to which has been added a lateral chain similar to that of L-mepromazine ("veractil"), one of the more powerful neuroleptic drugs.

The authors report a trial of 7162 RP on 102 psychiatric patients belonging to several diagnostic categories. Of 82 depressed patients, a good result was obtained in 62%, which is believed to be better than that achieved with other antidepressive drugs in hospital patients. The usual dose was 200 to 400 mg. per day, usually by mouth. Improvement was rapid and usually complete within 2 to 3 weeks. The drug was of most benefit in melancholic states and atypical and neurotic depressions. Symptomatic depression occurring in schizophrenia may also occasionally be relieved, while the schizophrenic symptoms themselves are rarely aggravated. With the doses employed subjective side-effects were not notable and the most disturbing features were neurological and psychiatric. In very rare cases a convulsive attack was seen, as also rarely was mild hypomania, but in a number of cases effects of overdosage such as dizziness, instability of the legs, hypotonia, dysmetria, or confusional states were observed. There are no precise contraindications, but there is thought to be some added risk in giving the drug to manic-depressive, arteriosclerotic, or hypertensive patients, the aged, and the habitual alcoholic.

Laboratory studies show that the toxicity of the drug is comparable with that of chlorpromazine. 7162 RP has both stimulant and sedative properties, which the authors relate to the optical isomers of the drug, the dextro- and the laevo-rotatory forms respectively. The sedative qualities are particularly attributed to the presence of the lateral chain. It is concluded that this "tranquillizing" effect, together with the degree of tolerance, usefully enlarges the scope of antidepressant drugs.

J. S. Bearcroft

1534. **Double-blind Study of Chlorprothixene (Taractan): a Panpsychotropic Agent**

T. N. KARN JR., B. T. MEAD, and J. J. FISHMAN. *Journal of New Drugs* [*J. new Drugs*] **1**, 72–79, March–April [received June], 1961. 1 fig., 1 ref.

The authors start by pointing out that chlorprothixene ("taractan") is chemically very similar to chlorpromazine, but differs from it in action in that it produces less apathy and drowsiness and has an antidepressant action.

A double-blind trial with chlorprothixene and a placebo was conducted on male patients at Wyoming State Hospital, Evanston, who had been in hospital for an average of 16 years. Of the 103 entering the trial, 18 suffered from chronic brain syndrome, 10 from manic-depressive psychosis, 68 from schizophrenia, 6 from sociopathic personality disturbance, and one from involutional psychotic reaction. The average age of the patients was 52·6 years. Thirty had previously been treated with other psychotropic drugs. The dosage of chlorprothixene, given by mouth to about one-half of the patients, ranged from 150 mg. to 600 mg. a day for 6 weeks. The results were assessed from clinical observations and a 9-item rating scale filled in by "trained charge aides".

An interesting finding was that the average results with chlorprothixene were not significantly better than those with the placebo for the first 3 weeks, after which, however, they showed a marked superiority. However, the average results with chlorprothixene were not very much better than those with the other psychotropic drugs previously used. Five of the 6 depressed patients showed improvement. Side-effects were negligible.

[The authors' claims of significant improvement with the drug cannot be accepted uncritically because the criteria of improvement are not well described and results of unavoidable environmental factors entering into the treatment were not assessed, and especially as most of the patients also improved with placebos.] *N. Rathod*

Dermatology

1535. **Pseudoxanthoma Elasticum and Angioid Streaks: a Review of 106 Cases**
P. J. Connor Jr., J. L. Juergens, H. O. Perry, R. W. Hollenhorst, and J. E. Edwards. *American Journal of Medicine* [*Amer. J. Med.*] **30**, 537–543, April, 1961. 4 figs., 16 refs.

In a review of the case records of 106 patients seen at the Mayo Clinic in the period 1931–58 with pseudoxanthoma elasticum, angioid streaks, or both, it was found that of 74 cases with typical skin changes, 63 (85%) had angioid streaks as well, while of 94 patients with angioid streaks, 32 (34%) had no cutaneous lesions, but 2 had osteitis deformans. There was a slight preponderance of women (41 to 33) among the 74 cases of pseudoxanthoma elasticum. In more than 70% of these cases the diagnosis was made during the fourth and fifth decades of life. Of 31 patients who could give an adequate family history, only 10 were aware of a similar disease in other relatives.

Angioid streaks are cracks in the lamina vitrea (Bruch's membrane) of the eye caused by degenerative changes in the elastic tissue composing this membrane; in nearly all cases both eyes are affected. Loss of central vision occurred in 69 (73%) of the present series. Of the 74 patients with pseudoxanthoma elasticum only, 12 (16%) showed clinical evidence of occlusive peripheral vascular disease at a younger mean age (42 years, range 16 to 66) than would ordinarily be expected, and 19 (26%) suffered from occlusive peripheral, coronary, or cerebral vascular disease; these rates are considered to be probably an under-estimate. The incidence of hypertension (23%) appeared to be relatively high. None of the patients with angioid streaks alone had coronary or cerebral arterial disease, and only one had peripheral arterial disease. In 10 patients with pseudoxanthoma elasticum and 2 with angioid streaks alone episodes of gastro-intestinal bleeding occurred, some of which were serious. In 3 cases histological study revealed degenerative changes of elastic tissue in the internal lamina of certain arteries, in which iron was present.

E. W. Prosser Thomas

1536. **The Histological Diagnosis of Dermatitis Herpetiformis, Bullous Pemphigoid and Erythema Multiforme**
J. Piérard and I. Whimster. *British Journal of Dermatology* [*Brit. J. Derm.*] **73**, 253–266, July, 1961. 18 figs., 9 refs.

The structural classification of blisters in which acantholysis usually plays no part, such as those of dermatitis herpetiformis and erythema multiforme, remains confused because the subepidermal position of the blisters gives such lesions a uniform appearance, and because recent work has resulted in a distinction being drawn between dermatitis herpetiformis and bullous pemphigoid (" parapemphigus "). Dermatitis herpetiformis has a specific histology which is quite different from that of bullous pemphigoid and bullous erythema multiforme. Further, the histology of bullous pemphigoid has much in common with that of erythema multiforme. The distinction between the two is made chiefly on the limited extent of the peribullous changes and the almost exclusively eosinophil infiltrate of bullous pemphigoid.

[This useful paper should be read by all interested in this subject. Its importance owes so much to the illustrations that it cannot be satisfactorily summarized.]

S. T. Anning

1537. **Is Eosinophilia of Diagnostic Importance in Dermatitis Herpetiformis?**
J. O'D. Alexander. *British Journal of Dermatology* [*Brit. J. Derm.*] **73**, 267–272, July, 1961. 26 refs.

A rapid review of the relevant literature shows that since 1895 it has been thought that in all patients with dermatitis herpetiformis there is an increase in the number of eosinophil granulocytes in the blood and skin, though many dermatologists have considered the eosinophil count to be unimportant in the diagnosis of this condition because in fact eosinophilia is often absent. At Glasgow Royal Infirmary the author, with the aim of clearing up this confusion, has carried out eosinophil counts on blood films from 33 healthy subjects, 33 patients with dermatitis herpetiformis, 15 with sulphonamide dermatitis, and 20 with other skin disorders.

Only the patients with sulphonamide dermatitis showed a significant increase in the eosinophil count. Further, the results of eosinophil counts performed by the " absolute " method showed no significant difference between 56 normal persons and 46 with dermatitis herpetiformis. Although the eosinophil count admittedly may be persistently raised to moderately high levels in severe cases of dermatitis herpetiformis, in general it is concluded that the level of circulating eosinophils is of no diagnostic importance, does not reflect the state of activity of the disease, and has no prognostic significance.

S. T. Anning

1538. **Follicular Mucinosis (Alopecia Mucinosa, Pinkus)**
H. Haber. *British Journal of Dermatology* [*Brit. J. Derm.*] **73**, 313–322, Aug.–Sept., 1961. 10 figs., 12 refs.

Mucinous degeneration of the follicles is found in a variety of unrelated dermatoses. It was first described by Kreibich in 1926, but in more detail by Pinkus in 1957. There is loss of hair, of the scalp or face particularly, in scaling erythematous patches. In this paper from St. John's Hospital for Diseases of the Skin, London, 12 cases of this condition are described, the affection in some instances being associated with itching. The aetiology is unknown, but the author suggests that it may be an expression of eczema of hair follicles comparable with eczema affecting the nails.

John T. Ingram

1539. **Investigations with Radioactive Isotopes in Dermatology**
A. SCOTT. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] No. 46, 22–35, 1961. 4 figs., 24 refs.

1540. **Studies in Contact Dermatitis. XIII—Diesel Coolant Chromate Dermatitis**
C. D. CALNAN and R. R. M. HARMAN. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] No. 46, 13–21, 1961. 22 refs.

Hexavalent chromate salts are widely used as oxidizers to prevent corrosion in the radiators of railway diesel engines, as well as in ice plants, refrigerator installations, air-conditioning systems, and in the aircraft industry. Of the three types of corrosion inhibitors—anodic, cathodic, and organic—chromate, which is of the anodic type, is considered to be the most efficient from the industrial point of view. But medically in many countries it is now realized that it is the most prone to cause dermatitis, through both its primary irritant action and also its allergenic effect; further, that such a dermatitis once produced tends to persist for years, resulting in a high degree of incapacity in the sufferer. In this paper from St. John's Hospital for Diseases of the Skin, London, 4 cases of chromate dermatitis are reported, all occurring in fitters working on diesel engines whose eruptions developed soon after their introduction to the new work and persisted long after their removal from contact with chromate. A review of the means by which the chromate is delivered to the locomotive engines revealed that there was frequent exposure of the workers to splashing and contamination with the chromate solution despite its being piped through the work yards.

Most railway systems, including British Railways, have now discontinued the use of chromate as an anti-corrosive and have substituted such alternatives as blended tannins (organic inhibitors) which, although slightly less efficient, are much safer than chromate. This is a decision to be welcomed by industrial dermatologists. *Allene Scott*

1541. **Erythema Neonatorum Allergicum**
B. DUPERRAT and A. J. BRET. *British Journal of Dermatology* [*Brit. J. Derm.*] 73, 300–302, Aug.–Sept., 1961. 2 figs.

The authors briefly review the literature, which dates from 1752, of so-called allergic erythema of the newborn and describe the outstanding features of the condition. Over a period of 4 months they observed the affection in 42 out of 400 newborn infants.

A lenticular papule or a pustule is surrounded by a zone of erythema 10 to 40 mm. in diameter and an eruption of such lesions, affecting chiefly the trunk and thighs, appears early, often within the first day of life. There is no general disturbance and the condition clears up within a few days without treatment. The pustules are sterile, contain a preponderance of eosinophils, and are related to sweat-duct orifices or sometimes follicles. There is often a blood eosinophilia of more than 7%. The cause of the affection is unknown. *John T. Ingram*

1542. **The Bacteriology of Acne Vulgaris in Relation to its Treatment with Antibiotics**
M. A. SMITH and P. M. WATERWORTH. *British Journal of Dermatology* [*Brit. J. Derm.*] 73, 152–159, April, 1961. 24 refs.

The bacteriology of acne vulgaris in relation to treatment with antibiotics was studied in 39 patients at St. Bartholomew's Hospital, London. From the majority of the lesions *Corynebacterium acnes* and *Staphylococcus albus* were cultured. *Staph. pyogenes* was not recovered from any of the specimens. The organisms were highly sensitive to penicillin and to some other antibiotics, including tetracycline, but were considerably less sensitive to streptomycin. Administration of antibiotics did not affect the sensitivity of the organisms and there was only doubtful evidence that the antibiotics penetrated the follicles.

The mode of action of antibiotics in the treatment of acne is discussed, but remains obscure. *John T. Ingram*

1543. **Onychia Due to Synthetic Nail Coverings: Experimental Studies**
P. D. SAMMAN. *Transactions of the St. John's Hospital Dermatological Society* [*Trans. St John's Hosp. derm. Soc. (Lond.)*] No. 46, 68–73, 1961. 4 figs., 8 refs.

The cosmetic industry recently introduced a number of base coat films for the finger and toe nails to replace the well-known and well-tried nail varnish. One of these, consisting of a phenol-formaldehyde resin plus synthetic rubber, produced a number of allergic reactions and was withdrawn from the market; a second nail covering incorporating a polyvinyl chloride resin plus adhesive has given rise to permanent dystrophic changes in the nails of many users and has therefore also been discontinued.

At the request of the manufacturers the author undertook an investigation at the Institute of Dermatology, London, to determine the cause of the latter effect, when six possibilities were considered. Three of these could be conclusively rejected, namely, allergy (since all patch tests gave negative results), deep penetration (excluded by microscopical examination), and interference with growth (since measurement of the growth of treated and untreated nails showed no significant differences). A fourth possibility, that is, bacterial action, could not be entirely discounted because many micro-organisms were observed microscopically between the film and the nail, without however any signs of inflammation. The two remaining factors, however, were considered to be important; these were " occlusion " of the nail by the film, with consequent interference with the normal exchange of moisture, leading to softening of the nail, and damage caused to the nail itself during the necessarily forcible removal of the very adherent adhesive film. The damage so caused appears to be cumulative and eventually becomes irreversible—hence such a cosmetic application should not be employed. *Allene Scott*

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

1544. **Hyperbilirubinaemia and Perceptive Deafness**
L. Fisch and A. P. Norman. *British Medical Journal* [*Brit. med. J.*] **2**, 142–144, July 15, 1961. 1 fig., 10 refs.

In this investigation of the relationship of hyperbilirubinaemia to perceptive deafness hearing tests were carried out on 50 children born in Queen Charlotte's Maternity Hospital, London, between 1953 and 1957 and who had shown neonatal jaundice; in 13 of them the bilirubin concentration had been at some stage over 20 mg. per 100 ml. Perfectly normal hearing was found in 41 and in 3 there was impairment of conduction, a finding, however, not relevant to the present study.

The remaining 6 had bilateral, perceptive, partial deafness and are considered in detail. Hearing was normal or slightly impaired in the lower range, but impairment gradually increased in the higher range, reaching a maximum defect between 2,000 and 4,000 c.p.s. Two of these children had severe athetoid cerebral palsy due to kernicterus resulting from Rh iso-immunization, while a 3rd was probably jaundiced as a result of ABO incompatibility; the remaining 3 had been premature infants with no evidence of iso-immunization. The authors remark that the maximum bilirubin concentration in 4 of these infants "was not very high and would be regarded by many as being well within the range of safety", the birth weights and maximum bilirubin concentrations (per 100 ml.) being 1,200 g. and 26 mg., 2,580 g. and 19 mg., 3,120 g. and 20·3 mg., and 680 g. and 15 mg. respectively. Inquiry showed that 5 of the 6 children had received large doses of vitamin K ("synkavit") ranging from 15 to 70 mg. and this is considered to have played a part in the production of the deafness. Experimental work on bacteria has shown that synkavit can uncouple oxidative phosphorylation, and this activity is also possessed by bilirubin. Hearing loss following hyperbilirubinaemia evidently results from damage to the cochlear nuclei, which in the newborn infant have a very high metabolic rate. The authors suggest that synkavit in excessive dosage may cause metabolic damage similar to that resulting from hyperbilirubinaemia and thus produce the isolated clinical condition of perceptive deafness.

F. P. Hudson

1545. **Nasal Carriage of *Staph. aureus* by Newborn Babies**
A. Cope, R. A. Shooter, S. M. Green, and W. C. Noble. *British Medical Journal* [*Brit. med. J.*] **2**, 329–330, Aug. 5, 1961. 8 refs.

It has been shown that babies who become carriers of staphylococci are, like adults, more liable to sepsis than those who do not become carriers.

At St. Bartholomew's Hospital, London, in a further effort to reduce the incidence of this carrier state, neomycin cream was applied daily to the noses of 221 newborn infants, in addition to the routine care of the skin with hexachlorophane soap and dusting powder. Of these 221 breast-fed babies, 38 (17%) were found to be carriers of *Staphylococcus aureus* on at least one day, but only 8 on 2 days, and only 10 had more than 2 positive swabs. There were no serious forms of sepsis, but minor forms occurred in 13% of the 38 babies who acquired staphylococci in the nose, compared with 2·7% of the 183 babies who did not become carriers, these maximum figures being based on the assumption that unswabbed septic spots were of staphylococcal origin. Sepsis did not occur in any of the babies before the 4th day. At the last examination before going home, normally about the 12th day, 16 of the infants were shown to be carriers.

Winston Turner

1546. **Carriage of Staphylococci in the Newborn: a Comparison of Infants Born at Home with those Born in Hospital**
R. E. O. Williams. *Lancet* [*Lancet*] **2**, 173–175, July 22, 1961. 6 refs.

A comparison is made of the nasal carrier rate for staphylococci between infants born at home and those born in hospital in the Hendon district of north-west London. Nasal swabs were taken from 502 babies born in hospital and 290 born at home and from their mothers at 8 to 14 days and again at 8 to 10 weeks after the birth and examined for *Staphylococcus aureus*. No specific antibacterial preparations such as powders or lotions were used. It was found that 65% of the babies born in hospital and 59% of those born at home were nasal carriers of staphylococci at 2 weeks, the rates for penicillin-resistant strains being 30% and 40% respectively. At 8 weeks the figures for carriers were 48·6% and 38·6% and for resistant strains 26% and 17·6%. The rates for the mothers were rather less, but comparable. Septic lesions were present in 16% of the babies and 8·3% of the mothers in the "home delivery" group and in 18% of babies and 12·1% of mothers in the "hospital delivery" group. There was no evidence of spread of infection from the midwives.

Winston Turner

1547. **Acidosis in Premature Infants Due to Lactic Acid**
H. I. Goldman, S. Karelitz, E. Seifter, H. Acs, and N. B. Schell. *Pediatrics* [*Pediatrics*] **27**, 921–930, June, 1961. 1 fig., 21 refs.

A follow-up report is presented from the Jewish Hospital, Long Island, New York, on the effects in premature infants of milk fortified with lactic acid. Sixteen premature infants were fed a proprietary lactic-acid milk preparation for 7 to 10 days and the results compared with those in 16 controls fed non-acidified half-skimmed

milk. The group receiving lactic acid gained less weight than the controls and developed acidosis. Similar results were obtained when half-skimmed milk to which lactic acid had been added was given.

It is concluded that lactic-acid milks should not be used for feeding premature babies. *John Fry*

1548. **Vomiting in the Early Days of Life**
W. S. Craig. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **36**, 451–459, Aug., 1961. 17 refs.

A clinical study of vomiting in the newborn baby was carried out at Leeds Maternity Hospital during the years 1954–60. Observations were made on 141 healthy male and 132 healthy female babies who had an isolated or occasional vomit (Series A), and also upon 260 male and 238 female babies who were ill (Series B). Vomiting occurred in 65% of babies in Series A; the onset was usually within 72 hours of birth and the vomiting rarely persisted for more than 2 days. The main causes of vomiting in the 498 babies in Series B were either (*a*) alimentary, due to feeding difficulties (113), gastric irritation from blood or meconium (37), pylorospasm (43), or alimentary obstruction (21), or (*b*) parenteral, due to abnormal stress of labour and/or delivery (168), infection (29), developmental anomalies (23), haemolytic disease (19), or neonatal cold injury (13). The time of onset, duration, forcefulness, copiousness, and colour of the vomit were of diagnostic help in many cases. *R. M. Todd*

CLINICAL PAEDIATRICS

1549. **The Clinical Picture and Treatment of Hypervitaminosis D in Early Childhood.** (Клиническая картина и лечение гипервитаминоза D у детей раннего возраста)
L. I. Beloborodova and A. A. Kedo. *Вопросы Охраны Материнства и Детства* [*Vop. Ohrany Materin. Dets.*] **6**, 48–51, July, 1961. 13 refs.

In the administration of large doses of vitamin D in the prophylaxis and treatment of rickets there is a definite danger of inducing hypervitaminosis D if control is not effective. The authors describe 29 children aged from 3 months to 2 years so affected in Leningrad. Nine were breast-fed, 10 breast-fed with supplementary feeding, 9 had artificial feeds, and one was on "toddler's" diet.

The chief symptom of hypervitaminosis D was anorexia with vomiting and constipation. The stools were dark yellow in colour and contained mucus and considerable quantities of neutral fat and fatty acids. In all cases there was loss of weight, dryness of the mucosa, thirst, and diminished turgidity of the tissues. Tachycardia, a systolic bruit, and dulling of the heart sounds were observed. Polyuria was present in all cases; the urine contained albumin, hyaline and granular casts, renal epithelial cells with fatty degeneration, and leucocytes and erythrocytes, the former in fairly large numbers. The liver was enlarged in most cases, but in 4 severely toxic children it was diminished in size. The skin was pale and dermatographism was present in some cases. Symptoms and signs of deficiency of other vitamins (A, C, B_1, and B_2), were often present. The bones of the cranial vault were thickened, and in 2 cases the anterior fontanelle was prematurely closed. Normochromic anaemia was common, the erythrocyte sedimentation rate was increased, the serum calcium level was raised, and the serum phosphate level lowered; in 10 cases the blood sugar content was increased.

Treatment in the first place was directed to combating toxaemia and dehydration; fluid with glucose was given by mouth or by intravenous injection together with vitamins A, C, B_1, and PP. At a later stage treatment was directed towards improving renal and hepatic function. Massage and movements were also employed. The diet was gradually broadened in scope to that corresponding to the patient's age. All the patients recovered. *L. Firman-Edwards*

1550. **Childhood Obesity: a Long-term Study of Height and Weight**
J. K. Lloyd, O. H. Wolff, and W. S. Whelen. *British Medical Journal* [*Brit. med. J.*] **2**, 145–148, July 15, 1961. 4 figs., 11 refs.

Although obesity in adults is a well recognized danger, its link with obesity in childhood has been little studied. In this investigation, reported from the University and the Children's Hospital, Birmingham, 98 obese boys and girls were studied prospectively over a 9-year period, height and weight being recorded initially in 1950 and at one or more of the three subsequent attendances in 1951, 1956, and 1959. Whereas at the first examination, as previously reported by Wolff (*Quart. J. Med.*, 1955, **24** 109; *Abstr. Wld Med.*, 1955, **18**, 512), these children were found to be taller than the standard for their age, at the end of the study their heights were below the expected level for both sexes. During the first period of the study (1950–51) the children were treated intensively with amphetamine sulphate and a 1,000-Calorie diet, with a resulting significant reduction in weight. However, a relapse occurred in the second (5-year) period in which the weight increase was statistically significant in the girls but not in the boys. In the final 3-year period no significant change in weight took place in either sex, most of the subjects having now reached the age of 18.

A comparison of the ultimate weight of those subjects who had been least overweight initially with the ultimate weight of those who had been most overweight showed that a highly significant difference had persisted. Of the 13 children grossly overweight at the first attendance, only one had returned to near normal weight, while of the 11 children who at the first examination were least overweight, only 3 were less than 20% overweight at the final examination, the remaining 8 being more than 45% overweight. It thus appears that obesity in childhood is likely to persist into adult life and because of its influence on morbidity and mortality calls for intensive treatment and long-continued supervision.

[To achieve this end a thorough personality screening might help in those children whose obesity is a psychosomatic disorder.] *David Morris*

1551. **Phenylketonuria. I. Dietary Management of Infants and Young Children**
W. R. CENTERWALL, S. A. CENTERWALL, P. B. ACOSTA, and R. F. CHINNOCK. *Journal of Pediatrics* [*J. Pediat.*] **59**, 93–101, July, 1961. 1 fig., 22 refs.

In this discussion of the dietary management of young patients suffering from phenylketonuria the authors describe their experience with " lofenalac ", a proprietary preparation which has a low phenylalanine content, supplies 80 to 90% of the patient's protein requirement, and also contains amino-acids, fats, and carbohydrates. It is in the form of a powder which can be made into a milk or mixed with food and is readily accepted by the children. The serum phenylalanine level should be kept between 2 and 6 mg. per 100 ml. Irritability and poor sleep did not usually appear until the levels were above 10 mg. per 100 ml. Nevertheless it is considered that during the 1st year of life the level should probably be between 2 and 4 mg. per 100 ml. It was noted that infants under 3 months old could tolerate over 20 mg. of phenylalanine per lb. (44 mg. per kg.) body weight daily, but those above one year of age only from 10 to 20 mg. per lb. daily. Of the phenylalanine required, from 30 to 50% was supplied by lofenalac; supplements of vitamins and iron were also given. In the authors' experience good control is most satisfactorily obtained when fruits and vegetables are the principal sources of the supplementary food required. Examples of diets suitable for various ages from birth to 7 years are tabulated.

Of the 10 children forming the basis of the study, 9 were treated as out-patients, none requiring admission to hospital, but close liaison with the mothers and the children's physicians was maintained. It is suggested that the diet should be continued as long as significant gains in mental level are recorded, but it is uncertain whether, and when, it is safe to discontinue it. The cost of lofenalac varies from 75 cents to 2 dollars a day, depending on the size of the child.

G. de M. Rudolf

1552. **Phenylketonuria. II. Results of Treatment of Infants and Young Children: a Report of 10 Cases**
W. R. CENTERWALL, S. A. CENTERWALL, V. ARMON, and L. B. MANN. *Journal of Pediatrics* [*J. Pediat.*] **59**, 102–118, July, 1961. 11 figs., 5 refs.

In this second paper [see Abstract 1551] the authors report the results obtained in 10 phenylketonuric patients who began to receive " lofenalac " as their basic diet when under 2 months of age in 4 cases, at 8 months in one, and between 1 and 3 years of age in 5. Vitamins and iron were added to the diet, and treatment was maintained for 6 months to 3 years. Intellectual development was tested approximately every 6 months, the Revised Stanford–Binet Scale being used for those aged 2 years or above and the Gesell Development Scale for those under this age (mental age).

It was found that in 5 cases the mental development rose, in one was stationary, and in 4 it fell. There was increase in alertness, responsiveness, and attention span, less irritability, better sleep, and rapid improvement in sitting, crawling, and walking. In regard to growth, the majority of the children developed as relatively short for their age but well proportioned. Serum phenylalanine levels before treatment ranged from 9·8 to 63·5 mg. per 100 ml.; during treatment they were kept so far as possible between 2 and 6 ± 2 mg. per 100 ml. The electroencephalogram, which had been abnormal in 6 of the children, became normal after $1\frac{1}{2}$ months to $2\frac{1}{2}$ years of treatment.

Mental retardation was prevented in all the children in whom the diet was started before 2 months of age. The 6 children receiving it between the ages of 8 months and 3 years showed an average increase in I.Q. of 25 points. The authors (who are enthusiastic about the ease of management of these phenylketonuric patients) conclude that mental retardation can be prevented by initiation of a low-phenylalanine diet in early infancy, although complete protection may not be afforded. Young children whose development is retarded before treatment show a variability of response, but probably are never completely restored to normal.

G. de M. Rudolf

1553. **Adenovirus and Intussusception**
P. S. GARDNER. *British Medical Journal* [*Brit. med. J.*] **2**, 495–496, Aug. 19, 1961. 7 refs.

A preliminary examination of the hypothesis that a precipitating cause of acute intussusception in children may be an adenovirus infection of the intestinal tract is reported from the United Hospitals and King's College, Newcastle upon Tyne. Faeces from 10 patients with intussusception and from 13 controls were examined on HeLa cells. If the response to the complement fixation test was negative neutralization with a rabbit herpes simplex antiserum was attempted, followed by inoculation on to the chorio-allantoic membrane of 10- to 12-day-old fertile hens' eggs. Monkey-kidney tubes were inoculated when available. An adenovirus was isolated from the stools of 6 of the 10 patients suffering from intussusception, but no adenovirus was isolated from the stools of the controls.

The author emphasizes that the series is small and that much more work needs to be done, but he postulates that adenovirus infection of the lymphoid tissue of the terminal ileum may precipitate imbalance of intestinal muscular contraction or give rise to swelling of the Peyer patches and thus cause intussusception.

Andrew M. Desmond

1554. **Clinical Recognition of Innocent Cardiac Murmurs in Children**
R. F. CASTLE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **177**, 1–5, July 8, 1961. 5 figs., 8 refs.

In this paper from Duke University School of Medicine, Durham, North Carolina, 5 innocent cardiac murmurs heard over the thorax and neck in children are described. They are the vibratory, or Still's, murmur, the pulmonary ejection murmur, the venous hum, the cardio-respiratory murmur, and the carotid bruit. The site of maximum intensity, timing, and other characteristics of the murmurs are discussed and they are compared with pathological murmurs with which they may

be confused. The author emphasizes the importance of differentiating innocent murmurs from pathological cardiac murmurs if unnecessary invalidism in the child and anxiety in the parents are to be avoided.

Marianna Clark

1555. **Primary Myocardial Disease in Infancy: Clinical Aspects**

J. Apley. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **36**, 366–372, Aug., 1961. 3 figs., 8 refs.

The term "primary myocardial disease" includes a group of diseases, commonest in infancy, in which the heart is chiefly involved, with cardiomegaly and electrocardiographic changes; it does not include congenital cardiac malformations and systemic diseases with slight cardiac involvement. Many cases are recognized only at necropsy. There may be a family history of a similar disorder. The case usually presents with a history of "chestiness" and a little cyanosis, with possibly attacks of vomiting.

In this series of 27 cases, all in children under 12 months of age, seen at the Royal Hospital for Sick Children, Bristol, examination revealed tachycardia, tachypnoea, moist lung sounds, and enlargement of the liver. In every case the heart was enlarged and in some a soft systolic murmur was heard. Fluoroscopy showed the left ventricle to be the chamber chiefly enlarged and cardiac pulsations were diminished. The electrocardiogram (ECG) showed the pattern of left ventricular strain. In all these cases blood and serological studies should also be carried out. The diagnosis is based on the detection of the enlarged heart and the suggestive ECG changes, but the latter alone are not diagnostic without other clinical evidence. Congenital cardiac malformations and systemic disorders must next be excluded. When the diagnosis of primary myocardial disease is established, then a differential diagnosis within the group should be made. The main forms of the disorder fall into two groups: Group 1 includes glycogen storage disease of the heart, an aberrant left coronary artery, and calcification or medial necrosis of the coronary arteries, while Group 2 includes myocarditis and endocardial fibroelastosis. In the last-mentioned the diagnosis is made by exclusion if the basic ECG pattern of infantile left ventricular strain is obtained together with cardiomegaly and there are no signs of other disorders. In myocarditis the left ventricular strain pattern may be seen, though here such changes are inconstant and often minimal. In glycogen storage disease of the heart the marked ECG changes may be diagnostic. In aberrant left coronary artery the ECG is characteristic and similar to that of anterior myocardial infarction in the adult. In medial necrosis or calcification of the coronary arteries the ECG changes may be those of left ventricular strain, but are not specific and require other investigations. In Group 1 there is no known effective treatment and the prognosis is poor, though ligation of the anomalous artery has recently been performed in 12 cases with moderate success at Johns Hopkins Hospital, Baltimore (Sabiston *et al.*, *J. thorac. cardiovasc. Surg.*, 1960, **40**, 321). In Group 2 the essence of treatment is early recognition and digitalization, together with administration of oxygen and antibiotics. It is wise to continue with digitalis, in gradually decreasing dosage, for a year after recovery.

J. M. Browne Kutschbach

1556. **Hypoplastic Anaemia in Infancy and Childhood: Erythroid Hypoplasia**

D. W. O'G. Hughes. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **36**, 349–361, Aug., 1961. 6 figs., 40 refs.

About 70 cases of a chronic progressive hypoplastic anaemia of unknown aetiology in children have been reported in the literature. Corticotrophin and corticosteroids have so far represented the most successful therapy. In the present investigation, reported from the Royal Alexandra Hospital for Children, Sydney, of 8 patients who developed this disorder during the first 18 months of life the diagnostic criteria were: (1) the presence of a chronic aregenerative anaemia with a relatively normal leucocyte and thrombocyte count; (2) exclusion of other underlying causes; and (3) a bone marrow showing failure of maturation of adequate numbers of erythroid cells.

Detailed descriptions of the cases show a lack of response to blood transfusions, remission under steroid therapy with relapse when this was withdrawn, and further remission when steroid therapy was combined with administration of vitamin B_{12} (cyanocobalamin) and folic acid. The presence of exomphalos, webbed neck, dwarfism, gross malformation of the urinary tract, prominent epicanthic folds, and blue sclerae in some of the children suggested a congenital origin.

In the peripheral blood the most prominent findings were profound anaemia and absence of reticulocytes, with moderate macrocytosis in most cases. The bone-marrow findings were variable, but when erythroblastic hypoplasia was present the morphology of the erythrocyte precursors was usually normal. When the proportion of erythroid cells was normal or increased defects of maturation in the form of multilobed and distorted nuclei, abnormal nuclear chromatin structure, scanty cytoplasm, and defective haemoglobinization of the nucleated erythrocytes became apparent, and during the early stages of steroid therapy megaloblastic erythropoiesis was sometimes observed.

The initial dose of prednisolone which produced remission was usually 20 to 30 mg. daily and the maintenance dose 5 to 10 mg. continued for 6 to 12 months. It is suggested that suboptimal response to adequate therapy should indicate the possibility of megaloblastic erythropoiesis.

Ethel Browning

1557. **Enlargement of the Thymus.** (К вопросу об увеличении вилочковой железы)

V. V. Guzeev. *Педиатрия* [*Pediatrija*] **40**, 54–58, July, 1961. 2 figs., 11 refs.

In an investigation of 1,487 children in Japan who were examined by pneumomediastinography Iotsucura found an enlarged thymus gland in 33·3% of children of day-nursery age as compared with 2·6% of those of pre-school age and 0·8% of those of school age. The present author has investigated 27 children all aged under one

year who showed signs of an enlarged thymus; of these, 5 had catarrh of the upper respiratory tract, 21 symptoms of a bilateral multifocal pneumonia, and one encephalopathy. Examination showed that 10 of the infants had an exudative diathesis, one erythrodermia desquamativa, 7 systemic enlargement of lymphatic nodes, while the spleen was palpable in 15. He points out that in cases of this type radiological investigation is most important. The enlarged thymus is usually asymmetrical and shows a shadow which is nearly always bell-shaped. A multiaxis investigation, including tomography and a comparison of the fluoroscopic and radiographic findings, is most essential. The appearances must be differentiated from those of a paramediastinal pleurisy and segmented atelectasis of the upper lobe of the lung. The thymus gland showed right-sided enlargement in 14 cases, bilateral enlargement in 7, and left-sided enlargement in only 3.

Three of the patients were treated with hormones, one receiving ACTH (corticotrophin) and 2 prednisone, as suggested by Vaccarini. In view of the very small number of cases the author refrains from commenting on the value of hormone treatment of enlargement of the thymus. *H. W. Swann*

1558. **Calcification of the Adrenal Glands in Young Children: a Report of Three Cases with a Review of the Literature**

J. STEVENSON, A. M. MACGREGOR, and P. CONNELLY. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **36**, 316–320, June, 1961. 3 figs., 18 refs.

The authors of this paper from Ruchill Hospital, Glasgow, describe the chance finding of bilateral adrenal calcification in 3 infants who developed pneumonia at the ages of 7 weeks, 18 months, and 2 years respectively. The known causes of such calcification include tuberculosis, septicaemia, tumours, cysts, lipoidosis, and trauma, but in these 3 patients no obvious cause was found. It seemed probable that haemorrhage in the perinatal period was the most likely aetiological factor. Investigation did not reveal any evidence of impaired adrenal function, but in view of the reports in the literature of the development in such cases of adrenal insufficiency later in life, especially as a result of stress, the progress of these patients is to be observed.

R. M. Todd

1559. **Study of Growth Patterns in Cerebral Palsy**

J. S. TOBIS, P. SATUREN, G. LARIOS, and A. O. POSNIAK. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **42**, 475–481, June, 1961. 3 figs., 14 refs.

Heights and weights of 86 cerebral palsied children were measured and found to be significantly below the norms used, and significantly lower than those of 86 non-handicapped children from the same geographic area, matched as to age, sex, and ethnic origin. Forty-five of the cerebral palsied patients had heights more than two standard deviations below the mean. Depression of stature was associated with greater severity of involvement as measured by the number of extremities involved, the ability to self-feed and to ambulate, but not significantly related to the intelligence quotient. Factors affecting growth in cerebral palsied children were discussed.—[Authors' summary.]

1560. **The Tryptophan Load Test in the Syndrome of Infantile Spasms with Oligophrenia**

B. D. BOWER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **54**, 540–544, July, 1961. 6 figs., 15 refs.

At the Children's Hospital, Birmingham, treatment with corticotrophin, prednisolone, or dexamethasone was given for at least one month, at or above the accepted dosage level for full effect in other diseases, in 19 cryptogenic and 14 symptomatic cases of infantile epilepsy with oligophrenia. The electroencephalogram (EEG) improved in 31 cases and the spasms stopped in 27. In two-thirds relapse took place after the cessation of treatment, this being most marked in the symptomatic group. In 3 out of 23 mental improvement was maintained (Griffiths's scale), but this rate was no better than in untreated cases.

The normal values for the tryptophan load test, which demonstrates pyridoxine deficiency, was found, in 22 children aged 2 months to 12 years, to be 5 mg. per 24 hours. Of 12 cryptogenic cases of infantile epilepsy, the results in 6 were above normal, but in 3 were only just above normal. Of 18 patients, 10 were given a second test during corticotrophin or dexamethasone therapy. In every case a reduction in xanthurenic acid output occurred. This acid is a breakdown product of tryptophan. Pyridoxine, 50 mg. daily, was given intramuscularly to 3 children. In one the spasms stopped and the EEG and clinical condition improved temporarily, in the second no improvement took place, although the response to the tryptophan load test became normal, and in the third the fits stopped and the EEG became normal (but one of the previous records had also been normal). *G. de M. Rudolf*

1561. **Systematic Ventriculographic Studies in Infants Born with Meningomyelocele and Encephalocele: the Incidence and Development of Hydrocephalus**

J. LORBER. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **36**, 381–389, Aug., 1961. 5 figs., 5 refs.

For the purposes of the present study the two chief aims of this investigation carried out at the Children's Hospital, Sheffield, were (1) to determine the incidence and degree of hydrocephalus in infants born with meningomyelocele or encephalocele and to relate this incidence to various clinical features; and (2) to determine what effect, if any, early operation on the meningomyelocele would have on the development of hydrocephalus and to determine the prognosis for those who had no hydrocephalus at the first examination. A total of 172 infants, 86 male and 86 female, all under 9 months of age on admission, who had been born with a meningomyelocele or an encephalocele were investigated, mainly by ventriculography.

The author's conclusions are as follows. " (1) There is an 80% incidence of hydrocephalus in association with meningomyelocele and encephalocele in infants. This

hydrocephalus can usually be detected in the first few days or weeks or life, even if the size of the head is not larger than normal, and other signs of increased intracranial pressure are not present. This was done by ventriculography through the fontanelle. (2) The incidence of hydrocephalus is far higher in infants whose meningomyelocele involves the lumbar region, than when it involves other sites, and is far higher if there is associated paraplegia; 96% of infants with paraplegia and a lumbar meningomyelocele, and 95% of infants whose head circumference was over the 90th percentile in the first few weeks of life had radiologically demonstrable hydrocephalus. (3) There is no evidence that repair of the meningomyelocele in the early neonatal period influences the development of hydrocephalus. No infant who did not have hydrocephalus at the first examination developed clinical or other evidence of hydrocephalus during a period of follow-up lasting up to 23 months. (4) It is desirable to perform routine ventriculography in babies with meningomyelocele as soon as possible after birth. This is of great prognostic value and is useful as a guide to treatment." *J. MacD. Holmes*

1562. **Intraventricular Administration of a New Derivative of Polymyxin B in Meningitis Due to *Ps. pyocyanea***
H. E. CLIFFORD and G. T. STEWART. *Lancet* [*Lancet*] **2**, 177–180, July 22, 1961. 17 refs.

At Queen Mary's Hospital for Children, Carshalton, Surrey, the authors have encountered 8 cases of *Pseudomonas pyocyanea* meningitis in infants. Five of these were treated with a new preparation of polymyxin B, this being the sodium salt of polymyxin B methane sulphonic acid. It is claimed that this drug is non-toxic on long-continued administration and is well tolerated both intraventricularly and intrathecally. For intraventricular injection 5,000 units was dissolved in 1 to 5 ml. of sterile water, and this dose was usually injected into each ventricle at 2- to 3-day intervals. All 5 of the treated patients, who were aged 1 to 6 months, also received 50,000 units of the drug 6-hourly by the intramuscular route. The concentration of the drug in the serum and cerebrospinal fluid (C.S.F.) was assayed and the sensitivity of the organism to polymyxin B and to other antibiotics was determined.

All 8 children had secondary meningitis. Three of them were treated with polymyxin B, chloramphenicol, and tetracycline, and 2 of these patients died. The 5 patients treated with the new preparation survived the acute phase of the illness, though 2 of them died later of hydrocephalus and urinary infection not due to *Ps. pyocyanea*. Of these 5 cases, the meningitis was due to a meningomyelocele with hydrocephalus in 4; the remaining patient had a secondary *Ps. pyocyanea* infection in a subdural effusion following aseptic meningitis after a craniotomy. In all 5 cases the ventricular and spinal C.S.F. was purulent. In 2 cases the C.S.F. became rapidly sterile after treatment, and in 2 others relatively early sterilization was followed by bacteriological relapse after intraventricular therapy had been interrupted, but on resumption of treatment the C.S.F. became sterile again. In the fifth infant all cultures remained positive until the 18th day. The C.S.F. cell count continued high for some time after the fluid became sterile, and the protein content rose to very high levels. In only 3 of the 5 cases was a normal cell count found at the time of the last examination, and the protein level was normal in only 2. In 2 cases the last recorded protein levels were 2·8 and 1·8 g. per 100 ml. on the 43rd and 30th days respectively after the beginning of treatment.

The maximum total dose of polymyxin (in 2 cases) was almost 20 million units. The level of polymyxin in the C.S.F. 2 hours after intraventricular injection was 100 units per ml. At 48 hours after injection a level of 8 units per ml. was detectable in one infant, but no drug was found in the C.S.F. in 2 others. In 2 infants whose ventricular C.S.F. was sampled one hour after intramuscular injection of 50,000 units no polymyxin was detected. No toxic side-effects were noted [though the rise in the C.S.F. protein content was noteworthy]. All the strains of *Ps. pyocyanea* in this group were sensitive to polymyxin B and its new derivative; the bacteriostatic concentration was 10 to 20 μg. per ml. and the drug had weak bactericidal action at 50 μg. per ml. No acquisition of drug resistance was encountered.

The authors reaffirm that polymyxin B is the drug of choice in the treatment of meningitis due to *Ps. pyocyanea* [though the claim that the new derivative is superior to the standard preparation is not substantiated]. The need for intraventricular treatment is stressed.

John Lorber

1563. **Milk Allergy in Infantile Atopic Eczema**
S. S. FREEDMAN. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **102**, 76–81, July, 1961. 16 refs.

A total of 50 eczematous children under the age of 2 years were studied at Rhode Island Hospital, Providence, to discover if any relation existed between the eczema and allergy to cow's milk. According to the author the diagnosis of milk allergy depends on repeated clinical trials. There must be a flare-up of the eczema within a short time of ingestion of cow's milk, previously withheld, and this effect must be reproducible. Repeated amelioration of the eczema after withdrawal of milk from the diet also suggests allergy. In all tests milk must be the only variable.

In all the 50 children examined skin lesions had appeared before the age of 4 months and a firm diagnosis of atopic eczema could be made with such evidence as family allergic history and the typical distribution and appearance of the lesions. When tested by the scratch technique 28% of the children were found to be sensitive to milk. In no case was cow's milk shown to be the exclusive factor in producing eczema, and it was the probable factor in only one case. It was suspected to be the cause by the parents of 12 children, but no evidence was found to support this. In the remaining 37 cases there was no evidence of milk sensitivity. In each of the last two categories 7 children gave a positive response to skin testing.

The author concludes that " in this selected series cow's milk seemed to exert very little influence upon the course of the eczema ". *E. H. Johnson*

Public Health and Industrial Medicine

1564. **The Changing Pattern of Poliomyelitis Observed in Two Urban Epidemics**
T. D. Y. CHIN and W. M. MARINE. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **76**, 553–563, July, 1961. 3 figs., 13 refs.

In 1959 two outbreaks of poliomyelitis occurred in Des Moines, Iowa, and Kansas City, Missouri, respectively. Careful observation of the epidemiological pattern showed that while this was similar in the two cities, it differed from that of previous epidemics, the change being attributed to the widespread use of Salk vaccine. In Des Moines there were 135 cases of the disease, 70 of which were of the paralytic form, and although other enteroviruses were isolated, poliomyelitis virus Type 1 was the predominant organism. In Kansas City 118 of the 210 cases of poliomyelitis were of the paralytic form, and again Type-1 poliomyelitis virus was the causal organism.

A series of maps and charts show that in both epidemics the poorer quarters of the towns were most severely affected. The attack rate in negroes in Des Moines was 20 times higher and in Kansas City 32 times higher than the attack rate in the upper-class white subjects, this difference being presumably related to the lower vaccination rate in the poorer areas. These findings were in direct contrast to those of investigations carried out before the introduction of Salk vaccination. Similarly, pre-school children were less well protected than school-children; the attack rate in pre-school children in Des Moines was 1½ times and in Kansas City 3 times that in children aged 5 to 9 years. In earlier outbreaks (in 1952 and 1954) the incidence of poliomyelitis was highest in children aged 5 to 9 years in the upper socio-economic groups.

The authors conclude on the basis of their observations that Salk vaccine appears to reduce the incidence of paralytic poliomyelitis in subjects under 40 years by about 80% and that high levels of vaccination may limit the spread of poliomyelitis virus in a community.

A. E. Wright

1565. **Observations on Excess Mortality Associated with Epidemic Influenza**
T. C. EICKHOFF, I. L. SHERMAN, and R. E. SERFLING. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **176**, 776–782, June 3, 1961. 4 figs., 20 refs.

In this paper from the Communicable Disease Center, U.S. Public Health Service, Atlanta, Georgia, the excess mortality of 86,000 attributed to the three waves of epidemic influenza that occurred in the U.S.A. during 1957–60 is analysed to identify groups at special risk.

More than two-thirds of the excess mortality occurred in persons aged 65 and over, the proportion increasing from slightly over 50% to 80% of the excess deaths from the beginning to the end of the observation period. Of these deaths, 85% were attributed to the cardiovascular-renal disease group (over 50%) and to the pneumonia-influenza disease group. On the basis of a 10% sample of death certificates from the National Office of Vital Statistics for the years 1959 and 1960 associations were found between influenza and pneumonia, arteriosclerotic heart disease, vascular lesions of the central nervous system, hypertensive heart disease, and generalized arteriosclerosis. An analysis of death rates per month for specific diseases from 1957 to 1960 showed that a small but consistent deficit of observed deaths compared with the number expected occurred several months after the 1957–8 epidemic. However, the amount of this "compensatory" deficit in each case was small and accounted for only a small proportion of the preceding excess. It is therefore suggested that "most victims of an influenza epidemic are those who might have lived considerably longer had influenza not claimed them, rather than severely debilitated patients in whom influenza is merely a terminal event". A marked increase was found in mortality from asthma and diseases of the respiratory system other than influenza and pneumonia, a moderate increase in that from diabetes mellitus and rheumatic heart disease, and a minor increase in that from cirrhosis of the liver, pulmonary tuberculosis, and chronic nephritis. An analysis of clinical studies in the U.S.A. and the Netherlands showed the pregnant woman also to be at risk.

Attention is again drawn to the fact that immunization of high-risk groups could materially reduce the mortality due to influenza.

Kurt Schwarz

INDUSTRIAL MEDICINE

1566. **Plutonium Inhalation Studies. II. Excretion and Translocation of Inhaled $Pu^{239}O_2$ Dust**
W. J. BAIR and B. J. MCCLANAHAN. *Archives of Environmental Health* [*Arch. environm. Hlth*] **2**, 648–655, June, 1961. 4 figs., 9 refs.

Radioactive plutonium (^{239}Pu) is being increasingly used for fuelling nuclear reactors, thereby increasing the probability of human contamination. In the present studies 4 mongrel dogs (A, B, C, and D) were exposed to plutonium dioxide introduced into a "lucite" chamber, the dogs inhaling the dust through a polyethylene mask connected by glass tubing to the chamber. Exhaled air from the animals passed through an electrostatic precipitator, an activated charcoal filter under negative pressure, and was finally exhausted to the outside through a packed cotton filter. The particle size of the dust ranged from 0·05 to 4 μ in diameter and the geometric mean by count was 0·60 μ and by weight 4·32 μ.

Two of the dogs (A and B) were killed 30 minutes after exposure, when 95% of the plutonium was found in the

respiratory tract, 75% being in the lungs and 20% in the trachea and upper respiratory passages. The remaining 2 dogs were kept in metabolism cages for 39 weeks. In the first of these animals (Dog C) 48% of the total dose was recovered in the faeces in the first 5 days following exposure, only 7% more being recovered in the rest of the period. Dog D eliminated 26% of the original dose in the faeces in the first 5 days and another 12% during the remaining 34 weeks. Excretion in the urine accounted for only 1·6% and 1·3% of the dose in Dogs C and D respectively. The total plutonium deposition was found by adding together the total amount excreted and the body content at the end of the experiment. Whole-body retention of plutonium could then be calculated by subtracting the cumulative excretion from the total deposition. The excretion curves show the presence of three components with biological half lives of 6·5, 25, and 1,460 days respectively in Dog C, and 3, 15, and 1,800 days in Dog D.

After 39 weeks both these dogs were killed by exsanguination and the tissues weighed and wet-ashed in nitric acid. Aliquots of ash dissolved in nitric acid were monitored on 1-inch (2·5-cm.) stainless steel plates with an alpha proportional counter. When the concentration of ^{239}Pu was less than 1×10^{-5} μc. per mg. of dried sample plutonium was extracted with thenoyl trifluoroacetone and monitored with a scintillation counter. Plutonium was found principally in the lungs, mediastinal lymph nodes, and faeces. The concentration in the lymph nodes exceeded that in the lungs by factors of 88 and 9 in the 2 dogs respectively. Within the lungs there were localized high concentrations of plutonium ("hot spots") which were demonstrated autoradiographically.

It is concluded that very little of the absorbed plutonium is transported in soluble form to tissues other than the lungs and associated lymph nodes. The latter receive a greater radiation dose than the lungs and might be considered to be the critical tissue. However, the distribution of plutonium in the lungs and lymphatic tissue is not uniform and evaluation of the biological effects of "hot spots" requires further investigation.

W. K. S. Moore

1567. **The Pathogenesis of Haemorrhagic Manifestations in Aluminium Workers.** (О патогенезе геморрагических явлений у рабочих алюминиевого завода)
Ju. P. Nikitin. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **5**, 33–36, July, 1961. 15 refs.

There are many reports in the literature that workers in aluminium factories frequently complain of bleeding from the gums and upper respiratory tract, but the aetiology of these manifestations has remained doubtful. In an attempt to shed light on the problem the author has investigated 500 persons working in the electrolytic department of a factory producing aluminium, a group of other workers employed elsewhere in the factory being examined as a control.

Of the total number examined, 22·4% complained of haemorrhagic manifestations in the course of their work, and it was noted that these occurred most often at times of inhalation of high concentrations of fluorine gas. Otorhinolaryngological examination usually gave negative results. In 42·4% of those examined telangiectasia of varying degree of the superficial vessels of the skin was found, and its severity increased with the length of employment in the factory; however, the cause of this phenomenon was not established. Investigation of blood coagulation factors and haematopoiesis revealed no significant abnormality while the patients were in hospital for the examination, but tests carried out on 70 workers at the beginning and end of a shift revealed an increased fragility of the capillaries of the oral mucosa and the skin of the forearm at the end of the shift. It was shown that the bleeding time was slightly prolonged, the clotting time increased, and the total serum calcium concentration was slightly diminished. The author suggests that the cause of the haemorrhagic manifestations is a toxic injury to the walls of the blood vessels where they are exposed to high concentrations of fluorine.

Basil Haigh

1568. **Treatment of Benzene Poisoning with Vitamin B_{12} and Folic Acid.** (Лечение бензольной интоксикации витамином B_{12} и фолиевой кислотой (экспериментально-клинические данные))
O. G. Vasil'eva, L. A. Zorina, and Ju. P. Sanina. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **5**, 30–33, June, 1961.

The therapeutic value of vitamin B_{12} and folic acid was tested experimentally in rabbits and rats and clinically in human subjects suffering from benzene poisoning. In 21 rabbits given subcutaneous injections of benzene there was a resulting decrease in the leucocyte and erythrocyte counts. In the 14 animals treated with vitamin B_{12} (1·5 μg. per kg. body weight daily for 10 days by subcutaneous injection) both the leucocyte and erythrocyte counts rapidly returned to normal, whereas in the 7 untreated control animals both counts remained low for a long period of time. Benzene poisoning was then produced in 60 white rats by inhalation (2 to 4 mg. per litre of air for 3 hours daily for 3½ months). In the 30 rats treated with folic acid daily for one month (0·1 mg. for animals weighing 250 g.) the lowered leucocyte and erythrocyte counts were rapidly restored to normal, whereas in the 30 control animals not given folic acid they remained at a low level.

In the clinical study vitamin B_{12} was used in the treatment of 35 patients suffering from chronic benzene poisoning, all of whom showed leucopenia, neutropenia, thrombocytopenia, astheno-vegetative reactions, and changes in the liver. The dose of vitamin B_{12} was 15 or 30 μg. daily, for a course of 300 to 1,500 μg. In all cases the leucocyte and erythrocyte counts increased and the haemoglobin level rose, while the patients also improved subjectively. The authors conclude that, on experimental and clinical grounds, vitamin B_{12} is effective in the treatment of benzene poisoning, and that from the experimental findings folic acid may also be of value.

Basil Haigh

1569. **Chronic Carbon Disulfide Poisoning.** [Review Article]
H. Brieger. *Journal of Occupational Medicine* [*J. occup. Med.*] **3**, 302–308, June, 1961. Bibliography.

Forensic Medicine and Toxicology

1570. **Possible Application of the Principle of Mixed Agglutination in the Identification of Blood Stains**
R. R. A. Coombs and B. Dodd. *Medicine, Science and the Law* [*Med. Sci. Law*] **1**, 359–377, July, 1961. 10 figs., 12 refs.

In the past the identification of blood stains as to their species origins or, in the case of human stains, their ABO group has been determined mostly by extraction followed by precipitation or inhibition.

The present paper from the University of Cambridge and the London Hospital Medical College describes a new approach and presents a model to be tried in parallel with existing methods. The method is based on the principle of mixed agglutination originally described by Coombs *et al.* (*Lancet*, 1956, **1**, 461; *Abstr. Wld Med.*, 1956, **20**, 89). Applying this principle, fibres which have been blood-stained are treated so as to have no intact erythrocytes and are then exposed to potent antisera. The antibody molecules combine specifically with the antigen receptors, which have become an integral part of the fibre. The fibres are then washed free of uncombined serum and exposed to indicator cells. Only cells containing the same antigen as is present in the fibres will adhere to the fibres. These clusters of cells can be seen under the microscope. So far, the method has been applied only to experimental stains for the A, B, H, and species antigens. Observations are needed on actual case material and further experimental work for other antigens should be undertaken.

[This is a new approach to the investigation of blood stains, a subject that has advanced little in comparison with our knowledge of blood groups and the methods of determining them.] *I. Dunsford*

1571. **Identification of Human Haemoglobin by an Immunological Method—Medico-Legal Applications**
M. Muller, G. Fontaine, P. Muller, and A. Gourguechon. *Medicine, Science and the Law* [*Med. Sci. Law*] **1**, 378–387, July, 1961. 6 figs., 17 refs.

At the Institute of Forensic Medicine, Lille, the authors prepared rabbit anti-human haemoglobin sera according to the technique described by Boivin and Hartmann (*Rev. franç. Ét. clin. biol.*, 1958, **3**, 48 and 50; *Ann. Biol. clin.*, 1959, **17**, 193). Using these sera by three different immunological methods, namely, those of Ouchterlony and Hartmann and Toilliez and Scheidegger's agar diffusion technique, they were able to differentiate human haemoglobin from that of other species tested. [No mention is made of tests on haemoglobins from other primates.] The method will detect both adult and foetal haemoglobin, but will not differentiate between them. It can be applied equally well to old stains or dried blood as to fresh material and is considered by the authors to be a very suitable technique to apply in forensic serology. *I. Dunsford*

1572. **Blows with the Shod Foot**
R. D. Teare. *Medicine, Science and the Law* [*Med. Sci. Law*] **1**, 429–436, July, 1961. 8 figs.

The author initially enumerates the not inconsiderable advantages of the shod foot as an offensive weapon and remarks on the increase of this type of assault, especially among young hooligans. He discusses, in the light of 5 cases, with photographs, the protean pattern of injury which may be thus inflicted. The correct recognition and interpretation of such injuries are stated to depend upon (1) their site, most usually areas of the head and neck inaccessible to attack with conventional forms of blunt weapon; (2) their tendency to be closely related to underlying bony structures; and (3) the disproportion commonly existing between external injury, which may be slight, and internal damage, which is frequently severe. *Gilbert Forbes*

1573. **Mushroom Toxins—a Brief Review of the Literature**
R. W. Buck. *New England Journal of Medicine* [*New Engl. J. Med.*] **265**, 681–686, Oct. 5, 1961. 6 figs., 33 refs.

1574. **Nerve Poisoning by the Organic Phosphates: the Role of the Anesthesiologist**
J. D. Michenfelder, H. R. Terry, E. F. Daw. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **40**, 397–403, July–Aug., 1961. 21 refs.

The organic phosphates are commonly used insecticides which are potentially lethal for man. Those most frequently encountered are tetraethylpyrophosphate (TEPP), hexaethyltetraphosphate (HETP), di*iso*propyl fluorophosphate (DFP), 0,0-diethyl-0-*p*-nitrophenyl thiophosphate (parathion), and 0,0-dimethyl diphosphate (malathion). Parathion has accounted for most of the reported cases of poisoning and is the most difficult to treat since its duration of action is significantly longer than that of the others. The major effect of these agents is a profound anticholinesterase activity which can be demonstrated by measuring the cholinesterase concentrations in the erythrocytes and the plasma; the erythrocytes provide a more accurate index of the severity of the poisoning. The clinical symptoms result from a combination of muscarinic and nicotinic effects as well as alteration of the central nervous system. Respiratory insufficiency usually predominates the clinical picture in the severe cases as a result of excessive secretions, bronchial constriction, neuromuscular block, and depression of the respiratory center. Therapeutic management includes large doses of atropine to reverse the muscarinic and central nervous system effects, and PAM (pyridine-2-aldoxime methiodide) to reverse the nicotinic effects. The anesthesiologist, because of his experience in handling respiratory problems in the operating room, should be well qualified to manage the complex problem presented by these patients.—[Authors' summary.]

Anaesthetics

1575. **Anaesthetic Experiences in 1,300 Major Geriatric Operations**

D. L. Scott. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **33**, 354–370, July, 1961. 28 refs.

The literature concerning geriatric anaesthesia and written in English since 1955 is briefly reviewed. A consecutive series of 1,300 major general surgical operations performed on 1,171 patients (665 men and 506 women) aged 70 years or more, is described [from St. Helens and South Liverpool Hospital Group]. The pre-operative complications are reviewed, especially with reference to mortality. It is seen that dehydration, shock and/or haemorrhage, cardiac decompensation, coronary sclerosis and previous coronary occlusion had the highest percentage of deaths.

Techniques are described. Muscle relaxant drugs were used in 44% of cases. Suxamethonium is preferred for shorter operations. Open ether was given by anaesthetic sisters to 56 patients (mostly for acute appendicitis) with only one death (from gas gangrene). Prostatectomies totalled 293, and presacral (parasacral) and subarachnoid analgesia, and general anaesthesia were used for them; 22 prostatectomy cases died. Refrigeration analgesia was used 8 times for thigh amputation in extremely poor risk patients, 4 of whom died. Experiences with halothane (59 cases) are described, including details of case histories which included one case of cardiac arrest with survival.

The overall mortality was 13·8% (180 deaths). This included 14 moribund patients who died shortly after operation. Absence of pre-operative complications reduced the mortality in 201 patients to 6·5%. Suggestions for technique are discussed, including a technique for spinal analgesia up to the tenth thoracic segment.—[Author's summary.]

1576. **Preanesthetic Medication with Intravenous Hydroxyzine: a Double-blind Study to Verify a Pilot Program and Uncontrolled Trial**

D. Bizzarri, F. E. Fierro, F. S. Latteri, J. Giuffrida. A. Schmookler, and H. C. Berger. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **40**, 378–383, July–Aug., 1961. 2 figs., 5 refs.

The authors report a study carried out on 621 adult female patients admitted to the Metropolitan Medical Center, New York, for emergency surgery, to whom hydroxyzine ("atarax") was administered intravenously one hour before operation and its effects assessed.

One group of 221 women undergoing dilatation and curettage were given 100 mg. of hydroxyzine in 20 ml. of saline, a variety of general and regional methods being used for anaesthesia. The premedication was considered to produce excellent calming effects in 92% and fair results in 7% of the patients. No appreciable change in blood pressure or pulse occurred in 92% of the patients. In a further 100 patients hydroxyzine or a placebo were given as premedication under double-blind conditions. Of the patients who received intravenous hydroxyzine the results were rated as being either good or excellent in 89%, compared with 47% of those who received the placebo. A report on the use of hydroxyzine given intramuscularly will be published later.

Mark Swerdlow

1577. **Cricoid Pressure to Control Regurgitation of Stomach Contents during Induction of Anaesthesia**

B. A. Sellick. *Lancet* [*Lancet*], **2**, 404–406, Aug. 19, 1961. 4 figs., 9 refs.

The entry of material from the stomach and oesophagus into the air passages is still a considerable hazard during the induction of anaesthesia, particularly for obstetric operations and emergency general surgery. The following simple method for controlling regurgitation during induction has been used at the Middlesex Hospital, London, on 26 patients in whom the risk was high. The stomach is emptied as completely as possible with an oesophageal tube, which is removed after a final aspiration just before induction. The patient lies supine with the head and neck extended. An assistant feels for the cricoid cartilage and holds it lightly between the thumb and second finger. During induction of anaesthesia the assistant presses the cricoid cartilage firmly backwards with the index finger; a nurse or midwife can easily be taught to do it. Pressure is maintained until intubation and inflation of the cuff on the endotracheal tube are completed.

Studies on the cadaver and on the anaesthetized and curarized patient indicate that cricoid pressure obliterates the oesophageal lumen at the level of the body of the fifth cervical vertebra. Not only is the regurgitation of material prevented, but the lungs may be ventilated by intermittent positive pressure, using a face-piece, without the risk of gastric distension. The author warns that active vomiting should not be controlled by cricoid pressure because of risk of damage to the oesophagus.

J. V. I. Young

1578. **The Expired Carbon Dioxide as a Continuous Guide of the Pulmonary and Circulatory Systems during Anesthesia and Surgery**

M. D. Leigh, J. C. Jones, and H. L. Motley. *Journal of Thoracic and Cardiovascular Surgery* [*J. thorac. cardiovasc. Surg.*] **41**, 597–610, May, 1961. 27 figs., 17 refs.

The authors of this paper from the Children's Hospital, Los Angeles, describe the monitoring of expired and inspired carbon dioxide during surgery under general anaesthesia in infants and children.

A Liston–Becker infra-red absorption analyser was used which was equipped with a special cell for fractional to-and-fro sampling of gases obtained by a polythene catheter inserted under the face-mask or 2·5 cm. into a port drilled in the angle piece of an endotracheal

tube. The catheters had an internal diameter of 0·034 inch (0·86 mm.), permitting the sampling, by suction, of 500 ml. of gas per minute. Satisfactory tracings were obtained with either an Esterline–Angus or a Texas Instruments recorder; the operator's own exhaled carbon dioxide was used to establish a standard deflection—approximately 5·5%. The authors state that more accuracy is possible if precise gas concentrations are used, but this is not considered necessary since in any event end-tidal samples are not truly representative of alveolar gas. They emphasize the importance of establishing a normal level for the expired and inspired gas of each patient, since this may vary considerably with the patient's disease.

Changes in expired gas content were considered with respect to carbon dioxide production, pulmonary blood flow, and alveolar ventilation, in that order. It was assumed that diffusing capacity remained unaltered; no corrections were made for alterations in barometric pressure, and only gross temperature changes were taken into account. The authors observed increased carbon dioxide production following rapidly induced metabolic alkalosis and a decrease during hypothermia. Changes in carbon dioxide excretion were then related to changes in pulmonary blood flow, because uniform alveolar ventilation was occurring. A cessation of excretion accompanied total circulatory occlusion and a decrease was observed during haemorrhage, deepening halothane anaesthesia, dislocation of the heart, and partial occlusion of the pulmonary artery. An increase occurred during blood transfusion, cardiac massage, and the use of a pacemaker. Vasopressor drugs appeared to produce no change. Finally, monitoring of the respiratory system showed that hypoventilation from drug depression, abdominal distension, chest splinting, or collapsed lung, also rebreathing due to increase in dead space, use of exhausted soda lime, or a faulty expiration valve caused a rise in the expired and inspired carbon dioxide content. A decrease in expired carbon dioxide indicated hyperventilation, but when this decrease was accompanied by an increase in inspired carbon dioxide there was partial airway obstruction.

[This paper undoubtedly calls attention to the dynamic status of carbon dioxide excretion revealed by continuous monitoring, and indicates that in some instances the appearance of an abnormality may be clearly interpreted, thus allowing early rational treatment.]

Raymond Vale

1579. **Circulatory and Respiratory Effects of Ether, Halothane and the Azeotrope Mixture: a Comparative Study in Children**

G. W. Black and S. H. S. Lovd. *Anaesthesia* [*Anaesthesia*] **16**, 324–332, July, 1961. 7 figs., 20 refs.

This study was carried out at the Royal Belfast Hospital for Sick Children on 50 children aged 5 years or more undergoing minor surgical procedures, of whom 10 received ether, 20 halothane, and 20 an azeotropic mixture of ether and halothane; the three groups were comparable in regard to mean age and body weight. Premedication was with atropine, 0·65 mg., given subcutaneously 30 minutes before induction. Anaesthesia was induced with 2·5% thiopentone, 4 mg. per kg. body weight, followed by nitrous oxide and oxygen (75:25%) and the volatile agent. EMO, "fluotec", and "azeotec" vaporizers were used to study ether, halothane, and the azeotrope respectively. Blood pressure, minute volume, and respiration rate were recorded every 3 minutes and the control level of ventilation was calculated from the Radford nomogram. An electrocardiograph was used to monitor cardiac rhythm and provided an accurate measurement of heart rate.

All results were based on observations made over a period of 10 to 20 minutes of stable anaesthesia before starting surgery. They showed that ether usually produced a mean arterial pressure above control level, that halothane did not produce any significant changes in pressure, while the azeotropic mixture produced a consistent and profound reduction in mean blood pressure. Normal sinus rhythm was usually present during ether anaesthesia; under halothane 3 patients exhibited arrhythmia, but with one exception normal sinus rhythm was the rule during azeotrope anaesthesia. All three anaesthetic agents increased the minute volume above control level, the change being least marked with halothane, and all three also produced similar increases in respiratory rate. The results are compared with the findings of other workers. *Mark Swerdlow*

1580. **Effect of Posture on Ventilation of Patients Anaesthetised with Halothane**

F. F. Wood-Smith, G. M. Horne, and J. F. Nunn. *Anaesthesia* [*Anaesthesia*] **16**, 340–345, July, 1961. 2 figs., 5 refs.

The effect of different postures on pulmonary ventilation was studied in 20 healthy adults undergoing non-abdominal operations at the Hammersmith Hospital, London. After premedication with pethidine and atropine (in most cases) anaesthesia was induced with 200 to 400 mg. of thiopentone, a cuffed tube inserted, and anaesthesia maintained with nitrous oxide and oxygen and 1 or 2% halothane. The measurements of ventilation reported were made immediately after the end of surgery, at which time the anaesthetic gas circuit was replaced by a non-rebreathing system incorporating a continuous flow spirometer. Control measurements were first made with the patient in the supine position, after which he was then changed as rapidly as possible to one of the following positions: Trendelenburg, gall-bladder, lateral, reverse Trendelenburg, lithotomy, prone, jack-knife, and kidney, each of which is defined and briefly described. Changes in ventilation were calculated as a percentage of the mean of the levels of ventilation before and after positioning.

It was found that the new level of ventilation was established as soon as the new position was attained and there was little change thereafter. Changes in respiratory lung volumes were derived directly from the spirometer tracing. Minute volume was considerably reduced in the kidney, prone, jack-knife, and Trendelenburg positions, while it showed an appreciable but lesser reduction in the gall-bladder, lateral, and reverse Trendelenburg positions. The lithotomy and prone positions

caused no significant changes. The findings are compared with those of similar previous studies.

Mark Swerdlow

1581. **The Safety of Neostigmine**
J. E. RIDING and J. S. ROBINSON. *Anaesthesia* [*Anaesthesia*] **16**, 346–354, July, 1961. 7 figs., 12 refs.

The authors have noted the absence of cardiac disturbance when neostigmine was used in patients in whom hyperventilation had been employed during anaesthesia. They therefore attempted to correlate the cardiac effects of neostigmine with changes in acid–base balance in 24 adult patients undergoing abdominal operations, all of whom preoperatively had shown a normal electrocardiogram (ECG), no clinical evidence of cardiac disease, and normal acid–base balance. Premedication was with morphine, 10 mg., and atropine, 0·6 mg., and anaesthesia was induced with thiopentone and maintained with nitrous oxide and oxygen, with full curarization, a circle absorber being employed and the respiration controlled throughout. Samples of venous blood were withdrawn at 15-minute intervals throughout surgery and again at the time of administration of neostigmine. The blood *p*H and CO_2 tension of the sample were measured, and the ECG recorded before, during, and immediately after anaesthesia.

Three different modes of respiratory control were used: (1) deliberate hyperventilation was carried out during maintenance of anaesthesia and until full reversal of muscular relaxation was obtained; (2) the patients were hyperventilated during maintenance but allowed to breathe spontaneously during reversal; and (3) respiration was controlled (without hyperventilation) during maintenance, and spontaneous respiration (without soda-lime absorption) was permitted during reversal. In all patients reversal of relaxation was effected by 1·2 mg. of atropine given intravenously, followed after 5 minutes by 5 mg. of neostigmine.

It was found that the cardiac effects of neostigmine were related to the manner of ventilation and to the degree of respiratory change in acid–base balance at the time of the neostigmine injection. In the patients in Group 3 some degree of respiratory acidosis occurred during the period when spontaneous respiration was returning and serious disturbances of cardiac rhythm were observed. It is recommended that assisted ventilation and absorption of carbon dioxide should be applied during the period of reversal.

Mark Swerdlow

1582. **Potentiation of the Neuromuscular Effect of Succinylcholine by Tetrahydro-amino-acridine.** [In English]
T. GORDH and Å. WÅHLIN. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **5**, 55–61, 1961. 3 figs., 18 refs.

Clinical tests have been made of a new anticholinesterase, tetrahydro-amino-acridine ("tacrin" or THA), reported to be a synergist of succinylcholine. In all 50 cases in which it was given, THA prolonged the effect of succinylcholine. The greatest advantage of this agent is that it reduces the quantity of succinylcholine administered per time unit. It therefore allows succinylcholine to be used in lengthy operations, without the necessity of doses apt to produce a dual block. Another advantage of THA is that it lacks the curaremimetic properties of hexafluorenium bromide, and therefore cannot contribute to the occurrence of such a block.—[Authors' summary.]

1583. **Controlled Hypotension in Neurological Surgery: Analysis of 482 Cases.** [In English]
M. TAPPURA, M. SLÄTIS, and H. TROUPP. *Acta anaesthesiologica Scandinavica* [*Acta anaesth. scand.*] **5**, 47–53, 1961. 1 fig., 10 refs.

The use of controlled hypotension with "arfonad" [trimetaphan] in 482 neurosurgical cases is analysed. There were 83 cases of aneurysm of the internal carotid artery, 57 cases of aneurysm of the middle cerebral artery, 101 cases of aneurysm of the anterior communicating artery, 58 cases of meningioma and 151 other brain tumours; 32 patients were operated upon for miscellaneous conditions.

It was impossible to pin-point hypotension injuries by statistical means; too many variable factors were involved. The case records of all patients with significant postoperative complications (usually neurological deficit) were examined; when no neurosurgical cause of the neurological lesion was found but complications during hypotension had arisen, the case was regarded as a possible hypotension injury. There were 10 such cases in the group with intracranial arterial aneurysm, but only one in the group of brain tumours (a patient with a meningioma).

It is concluded that hypotension may be particularly deleterious to the brain in cases where the cerebral vascular system is subjected to surgical intervention. Hypotension should not be used for any prolonged periods of time; it should not be used when deep-seated tumours necessitate prolonged surgical manœuvres with a consequent risk of retractor anaemia; nor should it be used for the control of intracranial pressure.—[Authors' summary.]

1584. **A Double-blind Study of a New Antiemetic Drug: SC–9387**
J. S. DENSON and W. E. ELESH. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **40**, 430–436, July–Aug., 1961. 1 ref.

This study of a new anti-emetic drug, SC-9387 ("mornidine"), was carried out on all patients over 10 years of age treated in the recovery room at Los Angeles County Hospital, California. Each patient received either 5 mg. of SC-9387 or physiological saline (control group) by intramuscular injection. The patient remained in the recovery room until he had fully recovered consciousness or the effects of a regional block (spinal or epidural) had worn off and until respiration and circulation were stabilized. The 1,197 treated patients and the 1,165 controls were statistically homogeneous as regards age, premedication, anaesthetic agents, type of operation, and skill of anaesthetist.

The incidence of vomiting (including retching) was 4·6% in the group who received SC-9387 and 9·7% in the control group, this difference being significant. The

incidence of vomiting in both groups was significantly higher in females than in males. A fall in blood pressure of more than 20 mm. Hg during the first 30 minutes after injection was significantly more frequent in the treated than in the control group. *Mark Swerdlow*

1585. **The Problem of Postoperative Pain**

B. R. J. SIMPSON and J. PARKHOUSE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 33, 336–344, July, 1961. Bibliography.

In this discussion, presented from the Radcliffe Infirmary, Oxford, the authors first recall that the origins of postoperative pain are related to the site and nature of the operation performed, but individual reactions are at least as important as the anatomical and physiological factors. In regard to peripheral pain there has long been controversy over the specificity of sensory nerve endings; recent work suggests a differentiation of sensory stimuli by means of alterations in the patterns of their discharges rather than by differences in the nature of the discharges *per se*. Visceral and deep somatic pain both present the same characteristic features, namely, an aching type of pain, poorly localized, which may be associated with nausea and vomiting; reflex muscle spasm itself is a potential new source of noxious stimuli. In respect of mechanisms in the central nervous system (C.N.S.), the long-standing conception of " pathways " for pain as rigid and independent systems conveying impulses which result in predictable responses has been dismissed by Gooddy as " but a figment of the observer's mind ". The present trend visualizes changing temporal and spatial patterns facilitated by the existence of multisynaptic internuncial neurone systems. By this mechanism many elements of the C.N.S. may be subjected to a prolonged bombardment of impulses arising from a single stimulus; these may persist long after cessation of the original stimulus and would thus explain intractable pain. A painful stimulus represents only part of the total efferent flow to the brain, and many factors determine the extent to which it obtrudes upon consciousness. One of the most important of these is the significance the person attaches to the pain experienced, and various individual and racial differences in reactions are cited. " Conditioning " can markedly raise the pain threshold, as has been shown in the training of secret service agents, but on the other hand mood, fatigue, and fear lower the threshold, as also may the behaviour of neighbouring patients in hospital after return from the operating theatre; in regard to this last much may be done to raise the threshold by means of a well-ordered ward, with reassurance from the nursing staff and adequate rest.

In assessing the efficacy of a line of treatment the self-limiting nature of postoperative pain, individual variations in reactivity, and its effects on coughing or movements must all be taken into account. The effects of morphine and similar drugs resemble those of frontal leucotomy in their effects in that such drugs tend to modify reactivity rather than prevent pain perception. They never provide complete analgesia and tend to produce respiratory depression and drowsiness, the dangers of which can be mitigated by amiphenazole or tetrahydroaminacrine; parasympathomimetic drugs prolong the action of the morphine group. The phenothiazine derivatives are said to reduce analgesic requirements by as much as one-third but, conversely, the use of promethazine or a barbiturate in premedication and thiopentone for induction have anti-analgesic effects. Local analgesic agents have long been used for postoperative pain, but wound infiltration and long-acting preparations have been discarded. Intercostal and paravertebral blocks are successful, but repetition of the procedure is unpleasant for the patient; however, intermittent extradural block and the use of an indwelling catheter overcome this difficulty and are shortly to be the subject of another paper by the authors. The infusion of anaesthetic agents by the intravenous route has been advocated, but the results are generally disappointing and large doses are liable to produce central depressant effects. Other methods cited include hypnotism and inhalation of trichlorethylene, the latter being of most value during the changing of wound dressings.

The authors conclude that insufficient attention is paid to treating postoperative pain and suggest that the usual hospital conditions in which patients are scattered throughout different wards make it difficult or even impossible to do so. Special recovery rooms near the theatre would enable the anaesthetist to prescribe selectively and more widely and would thus be a great advance. *Michael Kerr*

1586. **Postoperative Amnesia**

W. LAMBRECHTS and J. PARKHOUSE. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] 33, 397–404, Aug., 1961. 5 figs., 1 ref.

Patients were interviewed postoperatively and asked how soon they awoke from their anaesthetics. By selecting patients who were stated by the anaesthetist to be awake on leaving the operating theatre, it was possible to assess the duration of postoperative amnesia and to study the influence of some modifying factors.

Patients over the age of 60 showed an increasing tendency to be unaware of their actual time of awaking. Postoperative amnesia of more than 8 hours duration was common in old people. The use of hyoscine in premedication led to a significant prolongation of postoperative amnesia. In comparison with nitrous oxide and oxygen anaesthesia, equipotent ether–air mixtures produced greater degrees of postoperative amnesia, even when the patient was awake at the conclusion of surgery, and trichloroethylene–air mixtures produced very marked amnesia which occasionally lasted for days.

Patients operated on during the first 12 hours of the day tended to have rather longer periods of amnesia than those operated on during the second half of the day. However, most of the old patients in the series were operated on during the first half of the day. When postoperative drugs were administered during the amnesic period, the return of memory was significantly delayed. Even under the most favourable conditions, only approximately 40% of patients had clear and continuous memories from the time of their return to bed.—[Authors' summary.]

Radiology

1587. **Traumatic Diastasis of Cranial Sutures**
K. W. M. Grossart and E. Samuel. *Clinical Radiology* [*Clin. Radiol.*] **12**, 164–170, July, 1961. 16 figs., 8 refs.

A fracture of the skull may extend partly or wholly along a suture line and so be difficult or impossible to differentiate from simple diastasis. At the Royal Infirmary, Edinburgh, the authors have compared radiographs of the skulls of 250 patients without a history of head injury with those of 250 with head injury, the former group being examined in an attempt to establish a pattern of the normal variations in the width of the cranial sutures and to decide by measurement (principally of the lambdoid suture) what the upper limit of normal width is. In all but 3 of the 250 control cases the suture measured less than 1·5 mm. in width and the difference between the right and left halves of the lambdoid suture was never greater than 1 mm. Diastasis of the lambdoid suture therefore was regarded as being present if the suture measured more than 1·5 mm. (at 3 separate points more than 2·5 cm. apart) or if there was a difference of more than 1 mm. between the right and left sides.

Of the 250 patients with a history of head injury, 56 (22·4%) showed evidence of a fracture and/or diastasis, a fracture alone being present in 8%, diastasis alone in 10%, and a combination of fracture and diastasis in 4·4%. Diastasis was confined almost exclusively to the lambdoid suture, either bilaterally or unilaterally, the sagittal suture being involved in only one case. (It is noted, however, that diastasis of the sagittal or coronal suture has been observed occasionally since this report was prepared.) Towne's projection was found to be very valuable in demonstrating this separation of the lambdoid suture. Tests with a dried skull showed that rotation of the head up to 10 degrees from the true antero-posterior position did not materially affect the visibility of the sutures, so that slight variations in projection or positioning would not have falsified the findings significantly.

It is concluded that diastasis of a cranial suture may be demonstrated as frequently as a fracture and that fracture and diastasis may occur together. It is further suggested that suture diastasis gives an approximate guide to the site of maximum trauma and that it should be given the same medico-legal significance as the demonstration of a fracture line. *Arnold Appleby*

1588. **Traumatic Effusion of the Sphenoid Sinus**
D. F. Reynolds. *Clinical Radiology* [*Clin. Radiol.*] **12**, 171–176, July, 1961. 11 figs., 3 refs.

From the General Hospital, Southend-on-Sea, the author describes 14 cases of effusion into the sphenoid sinus and discusses the relation of this finding to fracture of the base of the skull. The effusion is diagnosed by the presence of a fluid level in the sphenoid sinus seen in a lateral radiograph taken with the head in the brow-up position and using a horizontal x-ray beam. This position is considered to be less disturbing for patients with serious head injuries as it avoids turning the patient's head to one side as would be necessary if a vertical ray were used. Of the 14 patients who exhibited this radiological sign, 8 died. Of the 6 survivors, 4 showed either radiological or clinical evidence of a fracture of the base of the skull. A review of 26 cases of head injury coming to necropsy at the hospital revealed that those exhibiting an effusion in the sphenoid sinuses showed rather more extensive fissuring in the base and more damage to the anterior part of the skull than those which had clear sphenoidal sinuses. In 2 patients whose radiographs showed occipital fractures as well as sphenoid effusion necropsy revealed additional fractures situated more anteriorly in the base of the skull. The site of the soft-tissue injury may be assumed to be the approximate site of maximum impact; on this assumption it was shown that the soft-tissue injuries in 11 of these 14 cases were situated mainly in the frontal region.

It is concluded therefore that the demonstration of an effusion into the sphenoid sinuses is a useful indirect sign of a fracture of the base of the skull and that such an effusion most commonly accompanies simultaneous injuries to the frontal region of the skull.

Arnold Appleby

1589. **Cerebral Angiography in the Diagnosis of Suprasellar Tumors**
N. E. Chase and J. M. Taveras. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **86**, 154–165, July, 1961. 21 figs., 11 refs.

Pneumography is superior to angiography in defining the size and shape of a tumour and its relationship to the third ventricle, but angiography is superior to pneumography in distinguishing the histological type of a tumour and differentiating it from an aneurysm. The angiographic signs of suprasellar tumour are discussed and an attempt is made to establish criteria for determining the direction and size of the growth without resort to pneumography. At Columbia Presbyterian Medical Center, New York, 103 patients with suprasellar tumours were examined by cerebral angiography; in one-half of these pneumography was also carried out. The diagnosis was confirmed in two-thirds of the cases at operation or necropsy.

It is pointed out that the most important vessels in the evaluation of these tumours are the cavernous, intracavernous, and supraclinoid segments of the internal carotid artery, the anterior choroidal artery, the posterior communicating and posterior cerebral arteries, and the proximal portion of the middle cerebral and the anterior cerebral arteries. In addition to aneurysms, pituitary adenomata can be diagnosed accurately by angiography, except in cases in which the sella is shallow and associ-

ated with extensive pneumatization of the sphenoid sinus. Lateral displacement of the cavernous sinus can also be shown except in the latter type of case. Posterior suprasellar tumours with no intrasellar component are the most difficult to diagnose by angiography. Bilateral angiography is usually necessary when studying suprasellar tumours to rule out an aneurysm, since there may be non-filling from one side even on cross-compression. *John H. L. Conway-Hughes*

1590. **Glomus Jugulare and Carotid Body Tumours**
T. D. HAWKINS. *Clinical Radiology* [*Clin. Radiol.*] **12**, 199–213, July, 1961. 14 figs., 41 refs.

This paper from Manchester Royal Infirmary reviews 15 cases of glomus tumour and 5 cases of carotid body tumour. It is explained that these tumours, so different clinically and radiologically, are associated in one communication because of their common histological appearance and common origin from so-called chemoreceptor tissue.

The clinical symptoms of tumours of the glomus jugulare depend partly on the site of origin of the tumour. Thus they may be mainly aural, when the patient complains of deafness, tinnitus, or vertigo, or perhaps blood-stained discharge from the ear; clinical examination may reveal a vascular polyp in the external auditory canal. Neurological symptoms may include difficulty in swallowing or speaking and examination may reveal cranial nerve palsies involving the 9th, 10th, or 11th nerves. Some cases present with a combination of oral and neurological symptoms. The role of radiology is to confirm the suspected clinical diagnosis by demonstrating bone destruction within the petro-mastoid and also to determine the extent of the tumour as evidenced by the extent of bone destruction or soft-tissue shadow or by angiography. The radiographic projections commonly used, which are described, include several projections of the petrous bone as well as tomography either in the antero-posterior or Stenver's position. The changes which may be seen on plain films vary from loss of translucency of the mastoid air cells to extensive destructive changes in the petrous bone. When the tumour arises in the jugular bulb these changes will appear only after erosion has occurred into the middle ear; the earliest destructive changes in these cases are seen in the region of the jugular fossa. Angiographic changes take the form of an abnormal vascular pattern within or adjacent to the area of bone destruction. The differential diagnoses are from middle-ear infection, tumours of the nasopharynx, acoustic neuroma, cholesteatoma, primary carcinoma of the middle ear, or metastatic disease.

In the 5 cases of tumour of the carotid body reviewed, 4 of the patients complained only of a mass in the neck, while the 5th complained of symptoms which were attributable to a tumour of the glomus jugulare, which was also present. The radiological investigation of most value in these cases is common carotid angiography, since this reveals the characteristic appearance of these tumours, as well as the site and spatial relationship to the carotid bifurcation. The demonstration of the patency or otherwise of the internal carotid artery and the presence or absence of cross-filling on the opposite side is of value in case ligation should become necessary during operative treatment. *Arnold Appleby*

1591. **The Tracheal Bronchus.** (Beitrag zur Kenntnis des Trachealbronchus)
A. HEIDENBLUT. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **95**, 77–85, July, 1961. 8 figs., 41 refs.

Occasionally, and almost without exception on the right side, a bronchus is seen to arise directly from the trachea at a point slightly above the bifurcation. This bronchus generally supplies the apex and possibly also other parts of the right upper lobe. The incidence of this occurrence is stated to be one or two cases per 1,000. It is recalled that tracheal bronchial branches are not unusual in the animal kingdom, and in the human embryo corresponding buds are by no means unusual, though they generally disappear later. A left-sided tracheal bronchus in man is very much rarer, largely because of the mode of arterial development in this area. As stated, the right tracheal bronchus supplies the apical segment of the right upper lobe, but in some cases the blood supply is from the subclavian artery and only in such cases is it correct to speak of a supernumerary lobe.

The author concludes with a description, complete with tomograms and bronchograms, of a case which came under his own observation. In this case the area in question showed hazy shadowing due to an early bronchial carcinoma. *F. M. Abeles*

1592. **New Approaches to Coronary Arteriography**
G. G. GENSINI, S. DI GIORGI, and A BLACK. *Angiology* [*Angiology*] **12**, 223–238, June, 1961. 23 figs., 13 refs.

After trying four of the known techniques of coronary arteriography, which are briefly described, the authors have developed, at St. Joseph's Hospital, Syracuse, New York, a technique which appears to be very satisfactory [although it is not made at all clear in how many patients they have so far used their new method].

The procedure is as follows. Under local anaesthesia a length of guided PE-280 polyethylene tubing 112 cm. long is introduced into the aorta via a percutaneous puncture of the femoral artery and advanced until the tip is level with the sinus of Valsalva. After 5 ml. of blood has been aspirated and a heparinized saline drip connected a small test dose of contrast medium is injected to check catheter position and sensitivity to the medium. Thereafter a small automatic syringe containing 0·4 mg. of acetylcholine in a strength of 0·1 mg. per ml. is triggered electronically by the electrocardiogram (ECG) so arranged that the injection is made in diastole by the patient's R wave. The ECG is inspected and if the succeeding R–R interval is less than 2 or 3 seconds further test injections are given, increasing the amount of acetylcholine by steps of 0·2 mg. up to a maximum of 1·2 mg. The correct dose of acetylcholine being thus determined this is then placed in a syringe connected to the catheter by a T tube, 40 ml. of " renografin 76 " in a Gidlung syringe being connected to the other limb. The amplified T wave of the patient's ECG triggers a

relay which delays the impulse for a period of time equal to the Q–T segment and thereafter activates a second relay which operates a solenoid and injects the acetylcholine. At the end of its travel the plunger of this syringe operates a microswitch which, after a short delay, triggers the contrast injection.

The authors state that the method is safe, reliable, and perfectly reproducible, and should enable a better selection to be made of patients for various medical and surgical procedures and also afford a reliable means of evaluating the results of therapy. *D. E. Fletcher*

1593. **A Contribution to Percutaneous Angiographic Technique in Cases of Tortuous Arteries.** (Zur angiographischen Technik der perkutanen Kathetermethode bei stark gebogenem Arterienverlauf)
D. Tille. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **94**, 782–784, June, 1961. 5 figs., 2 refs.

The author points out that if in the performance of percutaneous angiography the iliac arteries are very tortuous it frequently happens that the catheter with its guide wire cannot be negotiated round the sharp bends. In such cases he recommends that the guide wire be withdrawn a " few centimetres " so that the tip is then formed by the soft catheter only; if this is now pushed forward it will generally be found that the pliable catheter will negotiate the corner quite easily. This little manœuvre may be helpful in many cases. *F. M. Abeles*

1594. **The Examination of Patients with Suspected Perforated Ulcer Using a Water-soluble Contrast Medium**
G. Jacobson, C. J. Berne, H. I. Meyers, and L. Rosoff. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **86**, 37–49, July, 1961. 9 figs., 11 refs.

The authors of this paper from the University of Southern California School of Medicine and the County Hospital, Los Angeles, cite reports in the literature on the treatment of perforated peptic ulcer by aspiration of the stomach and without operation; these suggest a mortality rate which compares favourably with that in surgically treated patients. The criterion for conservative treatment is an ulcer which has sealed itself and ceased to leak, and to establish this a number of patients admitted to hospital with suspected perforated peptic ulcer were examined, a solution of " hypaque " (sodium diatrizoate) being instilled through a Levin tube into the stomach. The patients were screened and radiographs were taken in the supine and semi-erect positions. If no gross leak was observed a more detailed fluoroscopic examination was carried out and spot radiographs were obtained.

Of 120 patients examined, peptic ulceration was finally diagnosed in 98 (82%), who fell into four groups: (1) a pneumoperitoneum but no leakage (41); (2) a pneumoperitoneum with leakage (35); (3) no pneumoperitoneum and no leakage (16); and (4) no pneumoperitoneum with leakage (6). Conditions other than peptic ulcer were present in 22 patients, 9 of whom showed free peritoneal air and 13 did not. There was an error in diagnosis in 4 cases, 2 of gastric ulcer and 2 of duodenal ulcer. Pneumoperitoneum was present in 3 of these and the perforation had sealed. On examination with sodium diatrizoate no abnormality had been demonstrated. The presence of a sealed perforation was confirmed at operation. In the fourth case a subsequent gastro-intestinal examination revealed a duodenal ulcer.

Little correlation was observed between the length of history and the demonstration of a leak, nor did the delay between onset of acute symptoms and the time of examination have any bearing on the presence or absence of spontaneous closure. *A. M. Rackow*

1595. **Simple Benign Prepyloric Ulcer: the Possibility of an Unequivocal Roentgen Diagnosis**
B. S. Wolf and D. Bryk. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **86**, 50–61, July, 1961. 10 figs., 14 refs.

The authors do not concur in the widely held belief that most ulcers in the prepyloric part of the stomach are carcinomatous and cite published work which supports their view that the great majority are benign. They suggest certain criteria which, when applied to the radiological appearances of the lesion on barium-meal examination, should indicate with reasonable certainty the non-malignant nature of an ulcer. These are: (1) a single discrete crater lies within the prepyloric region (this being taken as within one inch (25·39 mm.) of the pylorus); (2) the ulcer is sited on the lesser curvature of the stomach; (3) the ulcer does not exceed 1 cm. in diameter; (4) the mucosal pattern is distinct and traceable to the margin of the lesion; (5) deformity of the prepyloric region is absent; and (6) a " niche " appearance is present, which they illustrate by a small undermined projection of barium.

Between 1953 and 1958, 141 patients were discharged from Mount Sinai Hospital, New York, with a diagnosis of simple gastric ulcer. A re-examination of these cases showed that in 26 the above criteria were fulfilled. Over a period of at least 12 months none of these 26 patients had displayed any signs of malignancy. In the same period 160 cases of carcinoma of the stomach were examined; in none of these, which included 84 cases of prepyloric lesions, were the criteria fulfilled.

The authors consider that if, in addition to applying the above criteria, the patient is re-examined after an interval of medical treatment the risk of mistaking a malignant lesion for a simple ulcer is minimal.
A. M. Rackow

1596. **The Roentgenologic Features of Carcinoma in Chronic Ulcerative Colitis**
J. R. Hodgson and W. G. Sauer. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **86**, 91–96, July, 1961. 8 figs., 4 refs.

In an attempt to clarify those radiological manifestations of carcinoma of the colon associated with ulcerative colitis which distinguish this condition from stricture or polypoid hyperplasia similarly associated, the authors, at the Mayo Clinic, reviewed 49 cases in which the radio-

logical appearances suggested that carcinoma of the colon was superimposed on ulcerative colitis. Of the 49 patients, 29 were ultimately shown to have carcinoma and ulcerative colitis, 2 had carcinoma without evidence of ulcerative colitis, 7 had a non-malignant stricture, and 4 had ulcerative colitis but no evidence of carcinoma. In the remaining 7 operation was not performed because other clinical findings did not support the diagnosis. The commonest site of the carcinoma was the transverse colon; multiple lesions were present in some cases. The authors state that any of the usual forms of carcinoma may be found associated with ulcerative colitis; the commonest is the constricting type, which accounted for more than half the cases in the present series. The appearances are similar to those in cases in which carcinoma occurs as an isolated lesion. In general the usual sharp delineation between the carcinoma and the normal bowel is not seen. In the so-called scirrhous type the bowel has a relatively flat appearance which is indistinguishable radiologically from the denuded mucosa of burnt-out chronic ulcerative colitis. When segmental narrowing of the lumen is present differentiation between carcinoma and stricture is difficult, the " flat " surface of the lumen appearing the same in both conditions. Although obstruction may occur with carcinoma, the only 2 cases of obstruction in the present series proved to be non-malignant. The lumen of the bowel at the region of carcinomatous growth is generally larger than that in cases in which carcinoma is an isolated lesion. The long constricting type of carcinoma will produce a more ragged and irregular lumen and a more constricting lesion than a localized polypoid hyperplasia.

John H. L. Conway-Hughes

1597. **Contribution of Radiology to the Pathology of Meckel's Diverticulum.** (Apport de la radiologie dans la pathologie du diverticule de Meckel)
R. FONTAINE, P. WARTER, R. WAHL, and F. WEILL. *Journal de radiologie, d'électrologie et de médecine nucléaire* [*J. Radiol. Électrol.*] **42**, 327–333, June–July, 1961. 7 figs., 31 refs.

Meckel's diverticulum is of some importance on account of the complications such as inflammation, perforation, haemorrhage, and volvulus to which it is subject. The x-ray examination is difficult and even if its presence is known from a previous operation it is not always possible to demonstrate its existence or position radiologically. The authors present from the University Surgical Clinic, Strasbourg, some examples, with illustrative radiographs, of comparatively small diverticula with a long neck, mostly lying alongside the inner aspect of the ascending colon. *F. M. Abeles*

1598. **Pancreatic Carcinoma and Its Early Roentgenologic Recognition**
J. O. SALIK. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **86**, 1–28, July, 1961. 43 figs., 31 refs.

In cases of advanced malignant tumour in the region of the head of the pancreas and duodenum the prognosis is poor, but long-term survival has been reported in cases operated on in the early stages. It is therefore important to recognize the often subtle changes visible in the routine radiograph which point to the presence of a mass associated with the first or second part of the duodenum. The tumours under consideration include carcinoma of the head of the pancreas, of the pancreatic duct, of the common bile duct, of the ampulla of Vater, and of the duodenum. In an outline of the symptomatology the author of this paper from Johns Hopkins Hospital, Baltimore, states that pain, contrary to the widely held belief, is an early feature and usually precedes jaundice. Loss of weight is also a constant finding and less constantly there may be diarrhoea of the steatorrhoea type, intestinal haemorrhage, and migrating thrombophlebitis. The blood sugar curve may be abnormal. In 49 out of 64 cases of proved carcinoma of the pancreas the condition was recognized before operation.

The author recommends study of the barium-filled stomach and duodenum in the prone and prone right-anterior oblique positions, with sometimes the addition of the supine left-posterior oblique position. Serial views are taken with and without local compression. The following features are described as being significant: (1) irregular contractions in some segments of the duodenum especially on the concave aspect of the loop; (2) changes in the mucosal pattern, which assumes a " brush-like " form; (3) the drawing out of local areas of mucosa into a pseudo-diverticulum; (4) displacement or compression of pre-existing duodenal diverticula; (5) a concave compression deformity or double concavity forming a mirror image of the figure " 3 " on the medial border; (6) a depression on the duodenum formed by a dilated common bile duct. With increase in size of the tumour the whole duodenal loop may become stretched and widened.

The differential diagnosis is from pancreatitis, various rare malignant conditions of the pancreas, annular pancreas, and tumours and post-bulbar ulcers of the duodenum. In another group the author briefly considers biliary neoplasms, retroperitoneal tumours, and aortic aneurysm. A number of cases of pancreatic carcinoma and the differential diagnosis are discussed.

A. M. Rackow

1599. **Medullary Sponge Kidney**
A. J. PALUBINSKAS. *Radiology* [*Radiology*] **76**, 911–919, June, 1961. 6 figs., 21 refs.

Medullary sponge kidney is an uncommon congenital abnormality of the renal pyramids with dilatation of collecting tubules and multiple small cysts. Over the 16-month period July, 1959, to October, 1960, a total of 29 patients (17 male and 12 female) suffering from this condition were seen at the University of California Medical Center, San Francisco, all except one being adults.

Medullary sponge kidney may be discovered accidentally or may present with recurrent renal infection or repeated urinary calculi. Usually, plain radiographs reveal the presence of multiple small calculi in both kidneys, lying in groups within the renal pyramids. On intravenous pyelography the cysts and dilated tubules may fill with contrast medium. Sometimes there may be pressure effects on adjacent minor calyces. The

radiological appearances may resemble those of renal tuberculosis and renal tubular stasis. The author states that there is no specific treatment for sponge kidney.

D. E. Fletcher

1600. **Medullary Sponge Kidney: Roentgen Diagnosis of Three Cases**
P. G. SECREST and T. A. KENDIG. *Radiology* [*Radiology*] 76, 920–926, June, 1961. 8 figs., 4 refs.

1601. **The Prone Position in Intravenous Urography for Study of the Upper Urinary Tract**
M. ELKIN. *Radiology* [*Radiology*] 76, 961–967, June, 1961. 15 figs., 9 refs.

A recumbent postero-anterior position is not generally used for excretory urography, but it may give valuable information. Urine containing the common contrast media is of higher specific gravity than non-opacified urine. In hydronephrotic kidneys and where there is stasis a layering effect occurs which may last up to 2 hours. In the normal kidney peristaltic activity of the calyces and pelvis prevents layering; horizontal levels in these structures therefore indicate stasis and atony. Because of the increased specific gravity of the urine the most dependent structures are seen best in the prone position; these are the inferior calyces and the ureter above the pelvic brim. The pelvic ureter may be best demonstrated in the erect position. To test the practical application of this, patients at the Bronx Municipal Hospital Center, New York, were given 50% sodium diatrizoate and radiographs were taken in the supine position with compression at 5 and 15 minutes, in the prone position at 25 minutes, and in the erect antero-posterior position at 30 minutes. The prone position was found to be useful in demonstrating the inferior calyces and pelvi-ureteral junction; in cases of undiluted and unobstructed ureter, however, the results in the prone position were disappointing.

John H. L. Conway-Hughes

1602. **Angiography of the Kidneys by Aortography or Selective Renal Angiography.** (Nierenangiographie durch Aortographie oder selektive Katheterisierung?)
D. TILLE. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] 94, 777–781, June, 1961. 3 figs., 13 refs.

In this discussion of the relative merits of renal angiography by selective catheterization or by aortography, presented from the Central Röntgen Institute of the City Hospital, Berlin–Buch, the author points out that admittedly selective renal angiography offers some distinct advantages, such as that there is no interference with the picture by other vascular shadows, a smaller amount of a less concentrated contrast agent can be used, and a better contrast is obtained between the lesser renal vessels and the renal substance.

On the other hand aortography still has the following undisputed advantages. (1) It is more economical, as cheaper catheters can be used; this may be quite a consideration, especially since a new catheter for each examination has been advised. (2) Selective renal angiography is time-consuming and entails more damage of the aortic wall, whereas aortography is quick and comparatively simple. (3) The duration and amount of exposure to radiation is less for all concerned. (4) Aortography shows both kidneys at once, and in addition visualization of the abdominal aorta may give important clues. The author also notes that selective renal angiography may occasionally produce confusing results, notably if there are supernumerary renal vessels or if the renal artery divides very early and the catheter has found its way into one branch; furthermore a renal artery may be so narrow that the procedure is just not possible. It has frequently been stated that by performing selective renal angiography at least one kidney is protected from potential damage, but this the author does not regard as of great importance. In any case, when there is disease of the excreting apparatus on both sides there is generally no indication for angiography.

F. M. Abeles

1603. **Micturition Cystourethrography with Automatic Serial Exposures: an Opinion on the Value of the Method.** [Monograph, in English]
L. K. HANSEN. *Acta radiologica* [*Acta radiol. (Stockh.)*] Suppl. 207, 1–139, 1961. 28 figs., bibliography.

RADIOTHERAPY

1604. **Technical Note on the Treatment of Angioma Simplex in Young Infants with Plaques Saturated with Radioactive Yttrium.** (Note technique: traitement des angiomes plans chez des enfants en bas age par des plaques imbibées d'yttrium^{90})
E. P. MALAISE, M. LAPIÈRE, R. LABEYE, and J. GUILLAUME. *Journal belge de radiologie* [*J. belge Radiol.*] 44, 277–287, 1961. 8 figs., 5 refs.

The authors emphasize the difficulty of treating the flat type of angioma simplex in infants, since this type does not tend to regress spontaneously and is liable to undergo tumourous and sometimes gravely disfiguring development. Moreover, the lesions are rather radioresistant, requiring from 4,000 to 5,000 r. to produce regression, or at least to prevent tuberose transformation. Working at the Dermatological Clinic of the University of Liège, the authors have found that the β rays of radioactive yttrium (^{90}Yt) are the most suitable form of irradiation. They use sheets of plastic material impregnated with an yttrium preparation; these are available commercially in two dose rates, namely, 3 r.e.p. and 15 r.e.p. per minute at the surface. The method of application is to obtain, under a light general anaesthetic, two plaster moulds of the child's face, from one of which is prepared a positive, while on the other an image of the lesion is copied by projection of a diapositive colour photograph. A paper pattern is prepared and an exact model of the lesion then cut from the yttrium-soaked plastic sheet. The child is again lightly anaesthetized, and the radioactive mould put in position and covered by the negative plaster mould to maintain firm and exact

contact with the lesion. The average treatment time is one hour. [No clinical results are quoted.]

E. Stanley Lee

1605. **Clinico-therapeutic Contribution to the Study of Tumours of the Parotid.** (Contributo clinico-terapeutico allo studio dei tumori della parotide)

F. COUCOURDE and F. A. PAOLINI. *Radiobiologia, radioterapia e fisica medica* [*Radiobiol. Radioter Fis. med.*] **16**, 141–156, 1961. 26 refs.

After reviewing the divergent views on the histogenesis and degree of radiosensitivity of parotid tumours the authors give details of the treatment and report the results in 27 cases of this condition seen at the Institute of Radiology, Pavia, since 1944. In 16 cases the tumour was of mixed type, in 2 an adenocarcinoma, in 6 carcinoma simplex, in 2 haemangio-endothelioma, and in one adenolymphoma. They conclude that as a rule, and especially in mixed tumours, the histological type is not a safe prognostic guide. They have found that a tumour presenting both the clinical and histological picture of an apparently benign lesion may later develop aggressive malignancy, even after apparently successful therapy. In all cases of parotid tumour, therefore, radical surgery is advisable, followed by postoperative irradiation; the technique used for the latter now consists in deep x rays given through a single direct field to a total dose of 2,500 to 3,000 r. Intact tumours or recurrences are treated by two tangential fields. *J. Walter*

1606. **Place of Radiotherapy in Treatment of Cancer of the Larynx**

M. LEDERMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 1639–1646, June 10, 1961. 9 figs., 6 refs.

The results of treatment by radiotherapy of 959 cases of laryngeal cancer seen at the Royal Marsden Hospital, London, during the period 1933–59 are analysed. Of these, 807 were previously untreated cases, and the author states that any method which allows the patient to preserve his life and at the same time conserve his larynx must be regarded as the treatment of choice. Radiotherapy alone can do this.

A new classification of the disease into glottic, subglottic, and supraglottic types is recommended, as each form behaves differently, has its own prognosis, and requires a different therapeutic approach. The cases are grouped into four stages and a table shows that in the latter part of the survey the percentage of early cases was higher and that of late cases lower than in the earlier years. Another table shows the value of classification in relating the site of the tumour to the very important prognostic factor of lymph-node metastases. The frequency of lymph-node metastases in supraglottic tumours as opposed to their extreme rarity in Stage-I glottic cases is pointed out. Cancer of the larynx is essentially a disease of middle-aged men. Only 7·5% of the author's cases occurred in women, who generally seem to seek advice earlier. The mean age for both sexes was 61·2 years, supraglottic tumours tending to occur earlier and subglottic tumours at a later age. Neither syphilis nor abuse of the voice seemed to be predisposing factors, but it was rare to find cancer of the larynx in the non-smoking male. Pre-malignant lesions of the larynx were not considered to call for radiotherapy.

Since early laryngeal cancer can be treated successfully by both radiotherapy and surgery the methods are competitive. The advantages of radiotherapy are, however, overwhelming in that operation may be avoided, a normal voice preserved, and the patient given two chances of survival. If surgery is chosen first and recurrence takes place postoperative radiotherapy in the presence of scar tissue is rarely of value. In the present series all early cases (Stages I and II) received radiotherapy. In advanced cases surgery was regarded as the treatment of choice for cases with laryngeal fixation, lymph-node metastases, or perichondritis and for recurrent cases after previous conservative surgery or radiotherapy. Sometimes a preliminary course of radiotherapy succeeded in obviating operation or, by shrinking the growth, made subsequent surgery easier. Recurrences in the tracheostome were less frequent in subglottic tumours after preliminary radiotherapy. If at 6 weeks after the completion of a course of radiotherapy the larynx was normal the patient was kept under observation. If the larynx was abnormal and the mucosa was not intact a biopsy was taken and if this was positive laryngectomy was performed. In advanced cases with an abnormal appearance of the larynx, despite negative biopsy, early surgery was considered advisable. Six weeks was considered a reasonable time for operation if necessary, as by then maximum tumour regression should have occurred and surgery would not be complicated by radiation fibrosis and bleeding.

Little preparatory treatment is needed for patients in good general condition with early carcinoma. Routine radiography of the chest with soft-tissue radiographs and tomographs is of prime importance. Routine preliminary biopsy was performed except in very frail or senile patients and tracheotomy was avoided in all except those *in extremis* as its performance complicates the technique of treatment and makes the prognosis worse. This is shown in the poor survival of 52 patients who had a tracheotomy. In all but 52 cases histological confirmation of the diagnosis was obtained. Where possible patients were treated as out-patients, but the elderly and debilitated, those with advanced disease, and those living at a distance were admitted. Oral sepsis was dealt with and a haemoglobin level of 60% or under corrected by blood transfusion. Treatment was given with a specially designed head and neck telecurie therapy apparatus to a total of 5,500 to 8,000 r. in 300-r. daily doses over a period of 6 to 8 weeks by protracted fractionation. Post-radiation complications were avoided by careful selection of the case and the method of treatment. Gamma-irradiation was considered preferable to x-irradiation.

The survival rates at 5 and 10 years respectively were as follows: glottic tumours, 60% and 36%; subglottic tumours, 36% and 29%; supraglottic tumours, 22% and 8%; Stage I, 81% and 61%; Stage II, 61% and 40%; Stage III, 22% and 8%; and Stage IV, 11% and 4%. Women in general did better than men, 73% of the for-

mer being free of cancer at 5 years and 50% at 10 years as against 45·4% of men at 5 years and 24·5% at 10 years. Early and squamous-celled lesions did better than undifferentiated neoplasms and the worst results were obtained with those patients from whom no section was obtained, all of whom ultimately died of the disease. The outstanding achievement of radiotherapy lay in the fact that nearly four-fifths of the survivors retained the larynx.

[This is an outstanding and comprehensive paper which should be read in the original by all who undertake the treatment of cancer of the larynx by any method.]

R. D. S. Rhys-Lewis

1607. **Radiation Therapy in Breast Cancer: Optimal Combination of Technical Factors; Analysis of Five-year Results**

N. G. DE MOOR, D. DURBACH, J. LEVIN, and L. COHEN. *Radiology* [*Radiology*] 77, 35–52, July, 1961. 5 figs., bibliography.

From the available literature it appears that the 5-year survival rate in breast cancer, all stages combined, is generally determined at the outset by the probability of widespread dissemination. The end-result is consequently unaffected by differences in treatment policy, except in so far as local recurrence of the disease is concerned. A statistical analysis of 469 patients treated by a variety of surgical and radiotherapeutic procedures and followed for 5 years confirms this view and indicates that in a proportion of patients surviving without metastases recurrent cancer in the regional nodes and chest wall will develop if adequate radiotherapy is not given to these areas.

The nature of the operation (local or radical mastectomy) has little if any influence on the outcome provided adequate irradiation is given to both the regional nodes and the chest wall. Inadequate radiotherapy or treatment limited to the peripheral nodes is associated with a high recurrence rate, particularly after local mastectomy. With radical operations, when treatment must be confined to the peripheral fields alone or otherwise limited, we have observed a high rate of irretrievable chest-wall recurrences.

In order to achieve significant reduction in the local recurrence rate, radiation therapy must be administered according to a dose–time combination of proved efficacy. We have found that 3,500 rads in 10 fractions over 4 weeks (H.V.L. 3 mm. Cu) is suitable for radical treatment to the primary site and regional nodes, or 2,700 rads to the chest wall in 9 fractions over the same period (H.V.L. 2 mm. Al). In the case of osseous metastases treated with small or elongated fields, single exposures of 1,500 rads each are uniformly effective.

The standard techniques (high-voltage tangential irradiation or treatment through direct superficial portals combined with peripheral fields to the regional nodes) result in few complications other than a low incidence (approaching 4%) of pulmonary fibrosis, generally affecting the apical or hilar regions and giving minimal symptoms. The quality of radiation or the arrangement of the fields appears to be relatively unimportant provided correct dosage is received by the whole affected area, in which case the recurrence rate among patients free of distant metastases is virtually zero.—[Authors' summary.]

1608. **Ankylosing Spondylitis**

J. S. FULTON. *Clinical Radiology* [*Clin. Radiol.*] 12, 132–135, April, 1961.

The results are analysed of x-irradiation in 573 cases of ankylosing spondylitis seen at the Radium Institute, Liverpool, between 1942 and 1958 and followed up for 5 years or more. The cases were grouped according to clinical stage of the disease as follows: Stage I (early) 167 cases, Stage II (moderately advanced) 227, and Stage III (advanced with poor posture and ankylosis) 179. The maximum incidence of the disease occurred in the third decade. While the aetiology of ankylosing spondylitis is doubtful, complications such as iritis, bronchitis, pulmonary tuberculosis, and peptic ulceration were most frequently seen in the later stages. The duration of symptoms before treatment varied considerably. Blood dyscrasias were found in 17 patients, including 12 in whom such blood changes had been present before treatment was started. Abnormalities developing after treatment included aplastic anaemia in one case, which proved fatal, and subacute myeloid leukaemia also in one case. Cancer developed subsequently in 7 cases.

Treatment was given in one of four ways—by trunk baths, by irradiation of the whole spine, or limited portions of the spine, or isolated joints or muscle insertions. There was improvement in 119 (72%) of the patients in Stage I, 141 (62%) in Stage II, and 81 (54%) in Stage III. The best results were obtained when the whole spine was irradiated and also when a high dose (2,000 r. in 2 weeks) was given. Further, the relapse rate was lower and the percentage of patients remaining symptom-free after 5 years was higher in patients given a high dose level than in those treated with a low dosage.

The author concludes that not only do the benefits of x-irradiation outweigh the risks of damage to the haematopoietic system, but that the risks of this treatment are negligible. *R. D. S. Rhys-Lewis*

1609. **Cobalt Radiation for Essential Hematuria**

G. L. MATHES and R. F. MAYER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] 177, 10–13, July 8, 1961. 4 figs., 10 refs.

Radioactive cobalt (^{60}Co) was used in the treatment of 8 cases of essential unilateral haematuria at the Baptist Memorial Hospital, Memphis, Tennessee. Of the 8 patients, 3 had venous calycine channels, one had increased capillary fragility, one probable varicosity of the renal pelvis, and one hypertension; the cause of haematuria in the remaining 2 patients was "totally unexplained". Treatment consisted in administration of about 1,500 r. to the affected kidney in 7 to 10 days, a ^{60}Co unit being used. Haematuria ceased in 6 patients, but in one of these, who had venous calycine channels, a return of symptoms after one year necessitated partial nephrectomy. In the remaining 2 patients (one with a venous calycine channel and one in whom the aetiology was unexplained) gross haematuria subsided, but microscopic haematuria persisted. *M. Sutton*

SUBJECT INDEX TO VOLUME 30

JULY—DECEMBER, 1961

References are to page numbers. An asterisk denotes title and reference only

AUTHOR INDEX TO VOLUME 30

JULY–DECEMBER, 1961

References are to page numbers. An asterisk denotes title and reference only

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